Practical Pediatric Therapy

Drug Therapy
Practical Management

Tenth Edition



Mohammed El-Naggar

Contents

How to Use Drugs

All drugs are poisons ... only the dose and the proper usage that determine what is therapeutic... and what is toxic. The most shameful act in medicine, apart from killing the patient, is to cause harm to a patient who is suffering from a self-limited disease. ***Good intentions towards patients are not enough ... knowledge and sense of responsibility are more important.***

Successful drug therapy necessitates certain precautions:

1. Accurate diagnosis: It is by far the most important single factor in planning for successful therapy. Empirical and symptomatic drug therapy are generally hazardous. On the other hand, accurate diagnosis sometimes renders drug therapy unnecessary.

2. True indication: Be sure that the drug is really indicated. Unfortunately, most people and many physicians still believe that the doctor's visit is not complete without a "prescription". In many situations, reassurance, understanding and kind explanation are much more effective than the "useless medications". It is important to remember that good physicians do not prescribe medications "on request". Many parents ask the physicians to prescribe a "vitamin" or "tonic" for their children and some physicians respond. The most serious effect of this attitude is psychological as it will intensify the wrong parental feeling that the child is abnormal and in need of medications.

3. Adequate knowledge: A good physician does not prescribe any medication unless he knows well about it. The generic name of the drug, the expected therapeutic effect and the possible side effects should be known. Doctors who understand and know about drugs are those who can choose drugs more skillfully and successfully than those who do not.

4. Optimum dosage: In most situations, drug dosage in pediatrics is calculated on the basis of mg/kg/day or mg/kg/dose. However, it is important to remember that in children above the age of 10 years (30 kg body weight), the adult dose should not be exceeded. This is particularly important in serious drugs as digoxin, theophylline and antiepileptics.

5. Appropriate route of administration: Oral route is the most convenient and most commonly used one. Parenteral drug therapy should be generally restricted to serious conditions and critically sick patients. Generally speaking, any patient who is in need of parenteral drug therapy is also in need of hospitalization. The common trend of using parenteral antibiotics for simple infections as tonsillitis, or bronchitis should be avoided. Parenteral antibiotic therapy should be limited to serious infections as meningitis, pneumonia and septicemia.

6. Duration of therapy: Drugs should be used for the least possible period. On the other hand, when an antibiotic therapy is indicated, treatment for 5 days is the minimum duration of therapy.

7. Number of drugs: Use the least possible number of drugs. Good doctors usually prescribe few medications. The efficiency of any physician is inversely proportionate to the number of drugs he prescribes. It is important to know that prescribing many medications will deprive the doctor from the chance to learn, and he will never know what is effective and what is not.

8. Drug interaction: When more than one drug are used, the problem of drug interaction should be considered. For example, calcium potentiates the toxic effect of digoxin and diuretics potentiate the nephrotoxic effect of aminoglycosides.

9. Drug mixtures: Generally speaking, don't respect any medicine that contains more than one active drug. Antidiarrheal mixtures and cough medicines are examples.

10. Simple explanation to parents: Parents should know the expected therapeutic effect and the possible side effects of any prescribed drug. This explanation is an important aspect of successful drug therapy. The parent's expectations are sometimes far from the actual expected response.

Emergency Medications

Dosage, proper usage and available preparations of emergency medications should be known to all doctors and nurses. As a rule, dosage should be calculated by 2 doctors to avoid accidental mistakes and nurses should be able to check dosage and notify doctors in case of suspicion.

According to the route of administration, emergency medications can be classified into I.V. drugs and inhalation drugs.

A) Intravenous drugs

These drugs are classified into the following groups:

1. Resuscitation drugs

Cardiopulmonary resuscitation is an emergency of 4 minutes. The following 2 drugs are given in the same sequence in case of cardiac arrest. Injections can be repeated every 10 - 15 minutes if resuscitative efforts are prolonged.

1. Sodium bicarbonate: 1 mEq/kg, I.V. Available preparations are ***Sodium bicarbonate 8.4% (1 mEq/ml) or sodium bicarbonate 5% (0.6 mEq/ml).*** Dosage is 1 ml/kg of 8.4% solution or 2 ml/kg of 5% solution.

2. Adrenaline: 0.01 mg/kg, I.V. Available preparation is ***Adrenaline amp (1 mg/ml).*** Dosage is 0.1 ml/kg of the diluted solution (1 ml + 9 ml saline).

2. Antiarrhythmic drugs

These drugs are used in serious life-threatening arrhythmias.

1. Atropine sulphate: 0.01 mg/kg, I.V. Available preparation is ***Atropine sulphate amp. (1 mg/ml).*** Practical dosage is 0.1 ml/kg of the diluted solution (1 ml + 9 ml saline). It is used in bradycardia.

2. Verapamil: 0.1 - 0.2 mg/kg, I.V. over 2 minutes. Available preparation is ***Verapamil or Isoptin amp. (5 mg/2 ml).*** Practical dosage is 0.5 ml/kg of the diluted solution (1 ml + 9 ml saline). It is used in severe symptomatic paroxysmal atrial tachycardia.

3. Lidocaine: 1 mg/kg, slow I.V. Available preparation is ***Lidocaine or Xylocaine vial (1 gm/50 ml).*** Practical dosage is 0.5 ml/kg of the diluted solution (1 ml + 9 ml saline). It is the drug of choice for ventricular arrhythmias.

4. Phenytoin: 3 - 5 mg/kg, I.V. over 5 minutes. Available preparation is ***Epanutin amp. (250 mg/5 ml).*** Practical dosage is 1 ml/kg of the diluted solution (1 ml + 9 ml saline). It is used as an alternative to lidocaine in treatment of ventricular arrhythmias.

3. Antihypertensive drugs

These drugs are used in treatment of hypertensive crisis.

1. Nifedipine: 0.25 - 0.5 mg/kg/dose ... sublingual or oral. Available preparations are ***Epilat or Adalat capsules (10 mg).*** The contents of the gelatin capsule are placed sublingually for immediate onset of activity. The dose can be repeated after 30 - 60 minutes when necessary.

2. Furosemide: 2 mg/kg, I.V. Available preparation is ***Lasix or Salex amp. (20 mg/2 ml).*** Practical dosage is 0.2 ml/kg. It can be used when the above drug is not available or not effective.

3. Methyldopa: 5 - 10 mg/kg, I.V. The available preparation is ***Aldomet amp. (250 mg/5 ml).*** Practical dosage is 1 - 2 ml/kg of the diluted solution (1 ml + 9 ml saline). In children weighing more than 10 kg, the dose is 1 - 2 ml of the undiluted solution, for each 10 kg. It is used when the above 2 drugs are not available. It lowers the blood pressure in 1 - 2 hours.

4. Hydralazine: 0.2 - 0.5 mg/kg, I.V. The available preparation is ***Apresoline amp. (20 mg/ml).*** Practical dosage is 0.1 - 0.25 ml/kg of the diluted solution (1 ml + 9 ml saline). It lowers the blood pressure in 30 minutes.

5. Sodium Nitroprusside: 0.5 - 5.0 mcg/kg/minute, continuous I.V. infusion. Available preparation is ***Niprid vial (50 mg/5 ml).*** For dilution and infusion rate, see antihypertensives. It is only used when the above 4 drugs are ineffective. As the drug is rapidly inactivated by light, the drip bottle and the tubing system should be covered with aluminum paper.

4. Inotropic drugs

These drugs are used to increase myocardial contractility in case of acute congestive heart failure.

1. Digoxin: 0.05 mg/kg (loading dose, divided into 3 doses, every 8 hours) **and 0.01 mg/kg** (maintenance dose, divided into 2 doses, every 12 hours). Available preparation is ***Digoxin Lanoxin amp. (0.5 mg/2 ml).*** Practical digitalizing dose is 2 ml/kg (divided as 1, 0.5 and 0.5) of the diluted solution (1 ml + 9 ml saline). It is important to know that the total digitalizing dose should not exceed the adult dose (1.5 mg). Digoxin is the drug of choice in acute congestive heart failure.

2. Dopamine:2-20 mcg/kg/minute, continuous I.V infusion. Available preparation is ***Intropin or Dopamine amp. (200 mg/5 ml).*** For dilution and infusion rate, see inotropic drugs. It is mainly used in severe congestive heart failure with cardiogenic shock. This serious drug should be only used in ICU where continuous monitoring of the heart is available.

3. Dobutamine: 2-20 mcg/kg/minute, continuous I.V. infusion. Available preparation is ***Dobutrex or Dobutamine vial (250 mg).*** For dilution and infusion rate, see inotropic drugs. It is used in cardiogenic shock and septic shock and can be used simultaneously with dopamine. It also should not be used except in intensive care units.

(See inotropic drugs, acute congestive heart failure and simple fever).

5. Anticonvulsants

These drugs are used to control the ongoing convulsive fit.

1. Diazepam: 0.3 - 0.5 mg/kg, I.V. over 3 minutes. The available preparations are ***Valium or Stesolid or Neuril amp. (10 mg/ 2 ml).*** Practical dosage is 0.1 ml/kg. The drug should not be diluted or mixed with other drugs. If convulsions cease during injection, don't complete the calculated dose.

2. Phenobarbital: 15 - 20 mg/kg, I.V. over 3 minutes. The available preparations is ***Sominaletta amp. (40 mg/ ml).*** Practical dosage is 0.5 ml/kg of undiluted solution. It is the drug of choice in neonatal convulsions. It is also used when diazepam is not effective within 10 minutes.

3. Phenytoin: 15 - 20 mg/kg, I.V. over 5 minutes. Monitoring of the heart during injection is important as serious heart block may occur. Available preparation is ***Epanutin amp. (250 mg/5 ml).*** Practical dosage is 3 ml/kg of the diluted solution (1 ml + 9 ml saline). It is used when diazepam and phenobarbital are not effective to control the ongoing convulsive fit.

With failure of the above 3 drugs (first-line drugs), the patient should be transferred to intensive care unit where more aggressive measures should be taken (see anticonvulsants and management of epilepsy).

6. Drugs to reduce increased intracranial pressure

These drugs are used in comatose patients with evidence of increased intracranial pressure. The aim of therapy is to reduce cerebral edema and to preserve brain functions. The main clinical indications are hypoxic ischemic encephalopathy, severe intracranial infections, Reye syndrome and surgically induced trauma.

1. Dexamethasone: 0.25 mg/kg/dose, I.V. every 6 - 12 hours. Available preparations are ***Decadron vial (8 mg/2 ml) , Fortecortin amp. (8 mg/2 ml), Epidron amp. (8 mg/2 ml), Dexonium amp. (8 mg/2 ml) OR Dexamethazone amp. (8 mg/2 ml),***

Practical dosage is 0.5 ml/kg/dose of diluted solution of 8 mg/2 ml (1 ml + 9 ml saline).

Dexamethasone is particularly useful in surgically induced trauma.

2. Mannitol 20%: 5 - 10 ml/kg, I.V. over 30 minutes every 6 hours. Available preparation is ***Mannitol 20% solution (bottle of 500 ml).*** Mannitol produces its therapeutic effect through increasing osmolarity of the blood and drawing fluids out of tissues (cellular dehydrating effect). Care should be taken to avoid volume overload.

3. Furosemide: 2 mg/kg/dose, I.V. every 12 hours. Available preparation is ***Lasix or Salex amp. (20 mg/2 ml).*** Practical dosage is 0.2 ml/kg/ dose. Furosemide may be used in severe cases in addition to dexamethasone and mannitol therapy.

It is important to remember that these drugs are used in conjunction with other measures as fluid restriction and may be mechanical ventilation.

(See neonatal convulsions and comatose child).

7. Drugs used in acute severe asthmatic episode

These drugs are used to relieve bronchospasm in patients with severe asthma.

1. Theophylline: 5 mg/kg/dose, I.V. ... over 10 minutes ... every 6 hours or by continuous infusion. Available preparations are of different concentrations. ***Minophylline N amp. (125 mg/5 ml=25 mg/ml) or Minophylline amp. (500 mg/5 ml = 100 mg/ml).*** Practical dosage is:

- 1 ml/kg of diluted solution of minophylline N 125 mg (1 ml + 4 ml saline).
- 0.5 ml/kg of diluted solution of minophylline 500 mg (1 ml + 9 ml saline).

2. Hydrocortisone: 5 - 10 mg/kg/dose, I.V. ... every 6 hours. Available preparations are ***Solu-cortef or Flebocortid or Hydrocortisone amp. (100 mg/ 2 ml)***. Practical dosage is 1 - 2 ml/kg/dose of diluted solution (1 ml + 9 ml saline).

8. Drugs used in acute metabolic conditions

These drugs are used in serious life-threatening acute metabolic conditions. Laboratory confirmation of the diagnosis before therapy is essential.

1. Sodium chloride 3%: 5 - 10 ml/kg, I.V. Rate of infusion should be as slow as 1 ml/minute. It is used to treat severe symptomatic hyponatremia with serum sodium below 120 mEq/liter. Each 1 ml/kg of this hypertonic saline solution will raise serum sodium level by about 1 mEq. (For accurate correction and details of therapy, see I.V. fluid therapy).

2. Sodium bicarbonate 5%: 2 - 4 ml/kg, I.V. over 10 minutes. It is used to treat acute severe metabolic acidosis with pH below 7.2 and serum bicarbonate below 10 mEq/liter. Each 1 ml/kg of this solution will raise serum bicarbonate level by about 1 mEq. (For accurate correction and details of therapy, see I.V. fluid therapy).

3. Calcium gluconate 10%: 1 ml/kg, I.V. over 5-10 minutes. Monitoring of the heart during injection is necessary and injection should be discontinued in case of bradycardia. It is used to treat tetany or hypocalcemic convulsions with serum calcium level below 7 mg/dl. The dose can be repeated if tetanic spasms or convulsions are not controlled (See neonatal convulsions).

4. Magnesium sulphate 10%: 1 - 2 ml/kg, I.V. over 10 -20 minutes. It is used to treat hypomagnesemic convulsions with serum magnesium level below 1.5 mg/dl. (See neonatal convulsions).

5. Glucose 25%: 1-2 ml/kg, I.V. It is used to treat hypoglycemic convulsions with blood glucose level below 30 mg/dl.

6. Regular Insulin: 0.1 unit/kg/hour. For dilution, rate of infusion and details of therapy, see diabetes mellitus.

9. Drugs used in coagulation defects

These drugs are used in bleeding disorders:

1. Vitamin K1: 5-10 mg, I.V. Available preparation is ***Konakion amp. (10 mg) or Konakion Pediatrics amp. (2 mg).*** Hemorrhagic disease of the newborn is the most common indication for use. It may be also tried in acute hepatic failure.

2. Heparin: 50-100 unit/kg/dose, I.V. every 4 hours. Available preparation is ***Heparin amp. (5000 unit/ml).*** Practical dosage is 0.1 - 0.2 ml/kg of the diluted solution (1 ml + 9 ml saline). It is only used in DIC associated with widespread cutaneous thrombosis as purpura fulminans.

10. Other drugs

The following drugs are used in different clinical situations.

1. Acetylsalicylic acid: 10 -15 mg/kg/dose, I.V. Available preparation is ***Aspegic injectable (500 mg/5 ml).*** Practical dosage is 1 ml/kg of the diluted solution (1 ml + 9 ml saline). It is indicated in case of hyperpyrexia (temperature above 41 .0°C).

2. Propranolol: 0.1 - 0.2 mg/kg/dose, slow I.V. Available preparation is ***Inderal amp. (1 mg/ml).*** Practical dosage is 1 - 2 ml/kg of the diluted solution (1 ml + 9 ml saline). It is mainly used in paroxysmal hypercyanotic attack in patients with congenital cyanotic heart disease.

3. Pancuronium: 0.1 mg/kg/dose, I.V. every 2-3 hours. Available preparation is ***Pavulon or Bromulex amp. (4 mg/2 ml).*** Practical dosage is 0.5 ml/ kg/dose of the diluted solution (1 ml + 9 ml saline). It is only used in ICU to induce respiratory paralysis in mechanically ventilated patients who are fighting the ventilator.

4. Naloxone: 0.01 mg/kg/dose, I.V. Available preparation is ***Narcan amp. (0.4 mg/ml).*** Practical dosage is 0.25 ml/kg of the diluted solution (1 ml + 9 ml saline). It is used as a respiratory stimulant. In neonatal respiratory depression due to opioids, the dose can be repeated every 2-3 minutes up to 3 times. After satisfactory response, the dose must be repeated every 1 - 2 hours, as long as opioid depression persists.

5. Prostaglandin E1: 0.05 – 0.4 mcg/kg/minute, continuous I.V. infusion. Available preparation is ***Prostin amp. (500 mcg/ml).*** The contents of the ampoule are added to 250 ml saline and are infused at a rate of 5-10 ml/hour in a newborn (about 3 kg). It is used to open the ductus arteriosus in newborns with congenital cyanotic heart disease.

6. Deferoxamine: 10 mg/kg/hour, continuous I.V. infusion. Available preparation is ***Desferal vial (500 mg).*** The contents of the vial are added to 100 ml saline and infused at a rate of 2 ml/kg/hour. It is used in accidental iron poisoning with serum iron level above 350 mcg/dl.

B) Inhalation drugs

These drugs are used in acute asthmatic attacks to relieve bronchospasm and they have the advantage of easy administration and rapid onset of action. These drugs can be used in emergency units and even at home.

In cooperative children above the age of 8 years, inhalation through the mouth with one of the commercially available inhalers is very useful but the child should be trained how to use it. Available drugs are either a beta 2 agonist (salbutamol, terbutaline or fenoterol) or anticholinergic drugs (ipratropium). Dosage of any preparation is 1-2 puffs/dose every 4-6 hours.

- **Salbutamol:** ***RI Ventolin inhaler (100 mcg/metered inhalation).***
- **Terbutaline:** ***RI Bricanyl inhaler (200 mcg/metered inhalation).***
- **Fenoterol:** ***RI Berotec inhaler (200 mcg/metered inhalation).***
- **Ipratropium:** ***RI Atrovent inhaler (20 mcg/metered inhalation).***

In infants and young children, inhalation through the mouth is impossible and the drug should by given by a "nebulizer" and a face mask to be inhaled through the nose. The 2 available drugs for nebulization are salbutamol and ipratropium. Salbutamol is the first and the most commonly used drug. Practical dosage is 0.25-0.5 ml of the drug added to 3-4 ml saline. Ipratropium can be added in severe cases. Practical dosage is 0.5-1.0 ml of the drug added to 3-4 ml saline. Treatment with both drugs is more effective than with either drug alone. Treatment can be repeated every 4-6 hours.

- **Salbutamol:** ***RI Ventolin OR Farcolin nebulization solution (5 mg/ml).***
- **Ipratropium:** ***RI Atrovent nebulization solution (250 mcg/2 ml).***

" بسم الله الرحمن الرحيم "

1

Antimicrobial Drugs

1. Antibacterial Drugs (Antibiotics).
2. Antituberculous Drugs.
3. Antiviral Drugs.
4. Antifungal Drugs.
5. Antiprotozoal Drugs.
6. Antihelmintic Drugs.

1. Antibacterial Drugs (Antibiotics)

Antibacterial families	Other antibacterial drugs
Penicillins	Chloramphenicol
Cephalosporins	Co-trimoxazole
Aminoglycosides	Aztreonam
Macrolides	Metronidazole
Carbapenems	Clindamycin and Vancomycin

*Tetracyclines should be avoided in pediatric practice. Repeated use of these drugs below the age of 8 years results in permanent discolouration of teeth enamel.

Mechanism of action

- **Beta lactam antibiotics** (Penicillins, cephalosporins, carbapenems and aztreonam) and **vancomycin** inhibit the bacterial cell wall synthesis.
- **Aminoglycosides** bind to the bacterial ribosomes, causing misreading of mRNA code and production of abnormal polypeptides.
- **Macrolides** and **chloramphenicol** interfere with protein synthesis through altering the function of ribosomes.
- **Co-trimoxazole** and **metronidazole** are antimetabolites. They block the essential metabolic events critical to microorganisms.

1. Penicillins

1. **Natural penicillins (Antigram-positive drugs)**
   - Benzylpenicillin (Penicillin G): 50.000 -100.000 unit/kg/day ... I.V. or I.M.
   - Phenoxymethylpenicillin (Penicillin V): 50.000 unit/kg/day ... oral.
2. **Penicillinase-resistant penicillins (Antistaphylococcal drugs)**
   - Cloxacillin: 50 - 100 mg/kg/day... I.V. or I.M.
   - Dicloxacillin: 50 - 100 mg/kg/day ... I.V. or I.M.
   - Flucloxacillin: 50 - 100 mg/kg/day ... I.V. or I.M.
3. **Broad-spectrum penicillins**
   - Ampicillin: 50 - 100 mg/kg/day ... oral, I.V. or I.M.
   - Sultamicillin (ampicillin + sulbactam): Same as ampicillin.
   - Amoxicillin: 25 - 50 mg/kg/day ... oral, I.V. or I.M.
   - Co-amoxiclav (amoxicillin + clavulanic acid): Same as amoxicillin.
4. **Broad-spectrum and antipseudomonal penicillins**
   - (Carbenicillin, Ticarcillin, Mezlocillin, Azlocillin and Piperacillin)
   - Piperacillin: 200 - 300 mg/kg/day ... I.V. or I.M.
5. **Fixed penicillin combinations**
   - Ampicillin + Cloxacillin
   - Ampicillin + Dicloxacillin
   - Amoxicillin + flucloxacillin

A) Natural penicillins

The antibacterial spectrum of these drugs is only limited to gram-positive infections. As they are destructed by penicillinase producing organisms, they are not considered as antistaphylococcal drugs. **Benzylpenicillin (penicillin G)** is *degraded by gastric acid and is poorly absorbed from the intestine, so, it is only* used as injections (I.V. or I.M.). **Phenoxymethyl penicillin (penicillin V)** is acid resistant and fairly absorbed from the intestine, so, it is given orally.

- **Benzylpenicillin: 50.000 - 100.000 unit/kg/day ... I.V. or I.M.**

The dose is divided into 4 equal doses (every 6 hours). In serious infections as staphylococcal pneumonia, staphylococcal meningitis or infective endocarditis, the dose can be increased up to 300.000 unit/kg/day.

Allergy to benzylpenicillin is rare so sensitivity skin testing is not needed.

* Available preparations are:

RI Penicillin G vial (1.000.000 unit).
RI Aqua-Pen vial (1.000.000 unit).

- **Procaine penicillin: 25.000 - 50.000 unit/kg/day ... I.M. only.**

The dose is given either once daily or divided into 2 doses (every 12 hours). It is a sustained-release preparation of benzylpenicillin with slow absorption and steady blood concentration over 12 -24 hours. This drug is rarely used nowadays. The painful injections and the risk of serious allergy are largely responsible for its limited usage. Moreover, oral phenoxymethyl penicillin is equally effective and safe.

* Available preparation is:

RI Penicillin procaine vial (400.000 unit).

- **Benzathine penicillin: 50.000 unit/kg ... I.M. only.**

The dose is repeated every 2 - 4 weeks.
It is another sustained-release preparation of benzylpenicillin that gives low blood concentration for few weeks. It is mainly used as a prophylactic therapy against streptococcal infection in patients with rheumatic fever or chronic rheumatic heart disease. Treatment is usually continued until streptococcal infection and rheumatic fever become unlikely to occur (usually after the age of 20-25 years). Again, oral phenoxymethyl penicillin (twice daily) is equally effective and safe.

* Available preparations are:

RI Durapen L.A vial (1.200.000 unit).
RI Lastipen LA vial (1.200.000 unit).
RI Retarpen L.A vial (1.200.000 unit).
RI Penicid L.A vial (1.200.000 unit).

(Sensitivity skin testing before every injection is important).

- **Phenoxymethyl penicillin (Penicillin V): 50.000 unit/kg/day ... oral.**

The dose is divided into 3 - 4 doses (every 6 - 8 hours). For prophylaxis against rheumatic fever, the dose is divided into 2 equal doses (every 12 hours).

It is the drug of choice for streptococcal pharyngitis.

* Available preparations are:

RI Cliacil syrup (300.000 unit/5 ml).
RI Ospen suspension (400.000 unit/5 ml).
RI Ospen OR Star-Pen tablets (1.000.000 unit).
RI Cliacil tablets (1.200.000 units).
RI Ospen tablets (1.500.000 unit).

B) Penicillinase-resistant penicillins

These drugs resist the destruction by penicillinase enzyme produced by some staphylococcal strains, so they are useful, as antistaphylococcal drugs, in serious infections as staphylococcal pneumonia and staphylococcal meningitis.

Although these drugs are effective against other gram-positive organisms (as streptococci and pneumococci), it is important to remember that benzylpenicillin is 20 times more active against these organisms.

The available drugs (**cloxacillin, dicloxacillin and flucloxacillin**) are rarely used alone because of their narrow spectrum. They are usually used in fixed combinations with ampicillin or amoxicillin to increase the spectrum of activity (see fixed penicillin combinations).

C) Broad-spectrum penicillins

These drugs are active against many gram-positive and gram-negative infections. The activity against gram-positive infections is midway between benzylpenicillin and penicillinase-resistant penicillins (benzyl penicillin is 10 times more active). These drugs are destroyed by penicillinase enzyme, so they are not considered as antistaphylococcal drugs. The activity against gram-negative organisms is mainly to H. influenza, E.coli and salmonella infection. They are not active against serious gram-negative infections as klebsiella and pseudomonas. These drugs are the most commonly used penicillins.

- **Ampicillin: 50 -100 mg/kg/day, oral or parenteral (I.V. or I.M.)**

The daily dose is divided into 4 doses (every 6 hours). The dose may be increased to 200 mg/kg/day (in septicemia) and to 300 mg/kg/day (in meningitis). The drug is generally safe. Two side effects may occur. Diarrhea may occur with oral preparations and skin rash may occur in some patients especially those with infectious mononucleosis.

* **Parenteral preparations** (vials for I.V. or I.M. injections) are mainly used in 2 conditions, gram-negative septicemia and bacterial meningitis.

RI Ampicillin vial (250 mg), (500 mg) and (1.0 gm).
RI Epicocillin vial (500 mg) and (1.0 gm).
RI Amfipen vial (500 mg) and (1.0 gm).
RI Farcocillin vial (250 mg), (500 mg).

* **Oral preparations** are mainly used for:

1. Respiratory infections as otitis media, sinusitis and bronchitis. It is important to mention that ampicillin is not a good choice in streptococcal pharyngitis as phenoxymethylpenicillin and erythromycin are therapeutically superior.
2. Urinary tract infection.
3. Salmonella infection (typhoidal and non-typhoidal).
4. It can be used empirically in "simple fever" when the clinical diagnosis of bacteremia is made (see simple fever, part II).

RI Ampicillin suspension (125 mg/5 ml), (250 mg/5 ml).
RI Epicocillin suspension (125 mg/5 ml), (250 mg/5 ml).
RI Amfipen suspension (125 mg/5 ml) and (250 mg/5 ml).
RI Ampicillin OR Epicocillin OR Amfipen capsules (250 mg).
RI Ampicillin OR Epicocillin OR Amfipen capsules (500 mg).

• **Sultamicillin (Ampicillin + Sulbactam):** Sulbactam is a beta lactamase (penicillinase) inhibitor. Its addition extends the activity of ampicillin to include beta lactamase producing strains of hemophilus influenza, E. coli, klebsiella pneumonia and staphylococcus aureus. Dosage is similar to ampicillin.

* Available preparations are:

* **Parenteral preparations**

RI Unasyn OR Unictam OR Sulbin vials 375 mg (250 mg + 125 mg).
RI Unasyn OR Unictam OR Ampictam vials 750 mg (500 mg + 250 mg).
RI Unasyn OR Unictam OR Ampictam vials 1500 mg (10000 mg + 500 mg).

* **Oral preparations**

RI Unasyn OR Unictam suspension 250 mg (167 mg + 83 mg).
RI Ampictam OR Sigmacyn suspension 250 mg (167 mg + 83 mg).
RI Unasyn OR Unictam tablets 375 mg (250 mg + 125 mg).
RI Ampictam OR Sigmacyn tablets 375 mg (250 mg + 125 mg).

(Sultamicillin tablets and suspension can be given every 12 hours).

• **Amoxicillin: 25 - 50 mg/kg/day, oral or parenteral (I.V or I.M.)**

The daily dose is divided into 3 doses (every 8 hours). The dose may be doubled in severe infections.

The antibacterial activity of amoxicillin is similar to that of ampicillin. Oral amoxicillin has some advantages over ampicillin. It has a better absorption and the incidence of drug-induced diarrhea is much less than that with ampicillin.

*** Parenteral preparations**

RI E-mox vials (250 mg), (500 mg) and (1.0 gm).
RI Amoxil OR Moxynil vials (250 mg) and (500 mg).
(Parenteral amoxicillin has no advantage over parenteral ampicillin).

*** Oral preparations**

RI Hiconcil OR Farconcil suspension (125 mg/5 ml) and (250 mg/5 ml).
RI Amoxil OR Amoxicid suspension (125 mg/5 ml) and (250 mg/5 ml).
RI E-mox OR Ibiamox suspension (125 mg/5 ml) and (250 mg/5 ml).
(All above trade names are also available as capsules, 500 mg).

- **Co-amoxiclav (Amoxicillin + Clavulanic acid):** Clavulanic acid is a beta-lactamase (penicillinase) inhibitor. Its addition extends the activity of amoxicillin to include beta lactamase producing strains of hemophilus influenza, E.coli, klebsiella and staphylococcus aureus (but not methicillin-resistant strains). Dosage is similar to amoxicillin. The Parenteral forms are given only by I.V. route

RI Augmentin OR Clavucin vial 600 mg (500 mg + 100 mg)… I.V. only.
RI Augmentin OR Clavucin vial 1.2 gm (1.0 gm + 200 mg) … I.V. only.

RI Augmentin OR Curam suspension 156 mg (125 mg + 31.25 mg/5 ml).
RI E-moxclav OR klavox suspension 156 mg (125 mg + 31.25 mg/5 ml).
RI Augmentin OR Curam suspension 312 mg (250 mg + 62.5 mg/5 ml).
RI E-moxclav OR Klavox suspension 312 mg (250 mg + 62.5 mg/5 ml).
RI Augmentin OR E-moxclav tablets 375 mg (250 mg + 125 mg).
RI Augmentin OR Curam tablets 625 mg (500 mg + 125 mg).

* Recently, the drug is available in a 7:1 ratio (7 amoxicillin to 1 clavulanic). With this ratio, it can be given twice daily (every 12 hours) with fewer side effects.

RI Megamox suspension 228 mg (200 mg + 28 mg/5 ml).
RI Megamox OR Klavox suspension 457 mg (400 mg + 57 mg/5 ml).
RI Augmentin OR Curam suspension 457 mg (400 mg + 57 mg/5 ml).
RI Hibiotic N suspension 230 mg (200 mg + 30 mg/5 ml).
RI Hibiotic N suspension 460 mg (400 mg + 60 mg/5 ml).
RI E-moxclav OR Klavox tablets 1000 mg (875 mg + 125 mg).
RI Augmentin OR Curam OR Hibiotic tablets 1000 mg (875 mg + 125 mg).

D) Broad-spectrum and antipseudomonal penicillins

These drugs have the same spectrum of ampicillin in addition to their anti-pseudomonal activity (mainly used in neonatal septicemia, mechanically ventilated patients or infections in immunologically compromised patients). The dose is **200 - 300 mg/kg/day … I.V. or I.M**, divided into 2-3 doses (every 8-12 hours). Piperacillin is the most potent and the mainly used drug.

- **Piperacillin:** *RI Pipril vial (2.0 gm) and (4.0 gm).*
  RI Tazocin vial 2.25 gm (2.0 gm + 250 mg tazobactam).
  RI Tazocin vial 4.5 gm (4.0 gm + 500 mg tazobactam).

E) Fixed penicillin combinations

Penicillin combinations are also available in one medication. The combination is made with a broad-spectrum penicillin (ampicillin or amoxicillin) and penicillinase-resistant penicillin (cloxacillin, dicloxacillin or flucloxacillin). The aim of such a combination is to make a broad-spectrum antibiotic with antistaphylococcal activity. Although the idea seems attractive, these combinations have a very bad taste and are usually rejected by most children.

* Available preparations are:

- **Ampicillin + cloxacillin**

  RI Ampiclox vial 500 mg (250 mg of each).
  RI Ampiclox suspension 250 mg (125 mg of each/5 ml).
  RI Ampiclox capsules 500 mg (250 mg of each).

- **Ampicillin + dicloxacillin**

  RI Dipenacid vial 500 mg (250 mg of each).
  RI Dipenacid OR Cloxapen suspension 250 mg (125 mg of each/5 ml).
  RI Dipenacid OR Cloxapen capsules 500 mg (250 mg of each).

- **Amoxicillin + flucloxacillin:**

  RI Flumox vial 500 mg (250 mg of each), 1000 mg (500 mg of each).
  RI Flumox OR Amoflux suspension 250 mg (125 mg of each/5 ml).
  RI Flumox OR Flucamox capsules 500 mg (250 mg of each).

2. Cephalosporins

First-generation (mainly for gram-positive infections)	
Cephalexin:	25 - 50 mg/kg/day ... oral or parenteral (I.V. or I.M.).
Cephradine:	25 - 50 mg/kg/day ... oral or parenteral (I.V. or I.M.).
Cefadroxil:	25 - 50 mg/kg/day ... oral.
Second-generation (broad-spectrum drugs)	
Cefamandol:	50 - 100 mg/kg/day ... I.V. or I.M.
Cefuroxime:	50 -100 mg/kg/day... I.V. or I.M. or oral.
Cefactor:	20 - 40 mg/kg/day ... oral.
Cefprozil:	20 - 40 mg/kg/day ... oral.
Third-generation (mainly for gram-negative infections)	
Cefotaxime:	50 - 100 mg/kg/day ... I.V. or I.M.
Cefoperazone:	50 -100 mg/kg/day ... I.V. or I.M.
Ceftriaxone:	50 - 100 mg/kg/day ... I.V. or I.M.
Ceftazidime:	50 - 100 mg/kg/day ... I.V. or I.M.
Cefixime:	8 mg/kg/day ... oral.
Cefpodoxime:	8 mg/kg/day ... oral.
Fourth-generation (Extended-spectrum drugs)	
Cefepime:	50 - 100 mg/kg/day ... I.V. or I.M.
Cefpirome:	50 - 100 mg/kg/day ... I.V. only.

Cephalosporins are bactericidal drugs structurally related to penicillins. The antibacterial activity is through inhibition of bacterial cell wall synthesis. Cephalosporins are generally **safe drugs.** Toxicity or adverse side effects are minimal when compared to other antibacterial drugs. Allergic skin rash and diarrhea may occasionally occur with oral preparations.

These drugs should be used with caution in patients with history of allergy to penicillins as cross-hypersensitivity may occur.

The antibacterial activity is different according to the generation.

A) First-generation cephalosporins

These drugs are mainly effective against gram-positive infections including penicillinase-producing staphylococci, so they are considered as **anti-staphylococcal drugs.** They are also effective against some gram-negative infections especially H. influenza and E. coli, so they are also effective in otitis media and urinary tract infections. The antibacterial spectrum of these drugs is essentially the same. The therapeutic indications are:

1. Respiratory infections: Streptococcal pharyngitis or tonsillitis (as an alternative to penicillin), otitis media, sinusitis and bacterial bronchitis.
2. Urinary tract infections.
3. Soft tissue infections as cellulitis, impetigo and other pyogenic infections.

- **Cephalexin: 25 - 50 mg/kg/day ... oral or parenteral (I.V. or I.M.).**

The dose is divided into 3 - 4 doses (every 6 - 8 hours).

Dosage may be doubled in severe infections.

* Available preparations are:

RI Ceporex suspension (125 mg/5 ml) and (250 mg/5 ml).
RI Ospexin suspension (125 mg/5 ml) and (250 mg/5 ml).
RI Keflex suspension (125 mg/5 ml) and (250 mg/5 ml).
RI Ibelix OR Cephalexin suspension (250 mg/5 ml).
RI Ceporex OR Keflex tablets (500 mg).
RI Ceporex OR Ospexin tablets (1000 mg).
RI Ceporex vials (500 mg) and (1.0 gm).

- **Cephradine: 25 - 50 mg/kg/day ... oral or parenteral (I.V. or I.M.).**

The daily dose is divided into 3 doses (every 8 hours).

- Available preparations are:

RI Velosef suspension (125 mg/5 ml) and (250 mg/5 ml).
RI Ultracef suspension (125 mg/5 ml) and (250 mg/5 ml).
RI Velosef OR Ultracef capsules (250 mg) and (500 mg).
RI Velosef OR Ultracef vials (250 mg) and (500 mg).

- **Cefadroxil: 25 - 50 mg/kg/day ... oral.**

  The daily dose is divided into 2 doses only (every 12 hours).

  RI Duricef suspension (125 mg/5 ml), (250 mg/5 ml) and (500 mg/5 ml).
  RI Curisafe suspension (125 mg/5 ml) and (250 mg/5 ml).
  RI Ibidroxil suspension (125 mg/5 ml) and (250 mg/5 ml).
  RI Biodroxil suspension (125 mg/5 ml) and (250 mg/5 ml).
  RI Longicef suspension (125 mg/5 ml) and (250 mg/5 ml).
  RI Cephadrol suspension (125 mg/5 ml) and (250 mg/5 ml).
  RI Duricef OR Curisafe OR Ibidroxil capsules (500 mg).
  RI Biodroxil OR Longicef capsules (500 mg).

B) Second-generation cephalosporins

These drugs are considered as **broad-spectrum drugs** with wide range of activity against both gram positive and negative organisms. The activity against gram-positive organisms includes the penicillinase producing staphylococci (antistaphylococcal drugs), while the activity against gram-negative organisms does not include pseudomonal infection, i.e. they are not antipseudomonal drugs.

* **Parenteral preparations** of these drugs are used in serious infections as septicemia, pneumonia, meningitis and peritonitis. The dose is **50-100 mg/kg/day...** I.V. or I.M., divided into 2-3 doses (every 8-12 hours).

* **Oral preparations** are mainly used in otitis media, sinusitis and urinary tract infections. The dose is **20 - 40 mg/kg/day**, divided into 2-3 doses.

- **Cefuroxime:** ***RI Zinnat suspension (125 mg/5 ml).***
  RI Cefumax suspension (250 mg/5 ml).
  RI Zinnat tablets (125 mg), (250 mg) and (500 mg).
  RI Zinnat vial (250 mg), (750 mg) and (1500 mg).
  RI Cefumax vial (750 mg) and (1500 mg).

- **Cefaclor:** ***RI Ceclor suspension (125 mg/5 ml) and (250 mg/5 ml).***
  RI Bacticlor suspension (125 mg/5 ml) and (250 mg/5 ml).
  RI Clorocef OR Cefaclor suspension (250 mg/5 ml).
  RI Bacticlor OR Cerviclor capsules (250 mg).
  RI Bacticlor OR Cerviclor capsules (500 mg).

- **Cefprozil:** ***RI Cefzil suspension (125 mg/5 ml) and (250 mg/5 ml)...50 ml.***
  RI Cefzil suspension (125 mg/5 ml) and (250 mg/5 ml)...75 ml.
  RI Cefzil tablets (250 mg) and (500 mg).

C) Third-generation cephalosporins

The antibacterial activity of these drugs is mainly directed to gram-negative infections. Although these drugs are also effective against streptococci and staphylococci, they are not considered as antistaphylococcal drugs.

Parenteral preparations of these drug are also effective against pseudomonas (antipseudomonal drugs), so they are similar to aminoglycosides with the advantage of being safe drugs. They are mainly used in serious infections, as septicemia, pneumonia, meningitis and peritonitis. The dose is **50-100 mg/kg/day**... I.V. or I.M. Cefotaxime and cefoperazone are given every 12 hours.

Ceftriaxone is given as a single daily injection. Ceftazidime is the most effective against pseudomonas and also the most expensive drug.

- **Cefotaxime:** *RI Claforan vial (250 mg) and (500 mg) and (1.0 gm).*
  RI Cefotax vial (250 mg) and (500 mg) and (1.0 gm).
  RI Ceforan OR Cefaxim OR Foxime vial (500 mg) and (1.0 gm).
- **Cefoperazone:** *RI Cefobid vial (500 mg) and (1.0 gm).*
  RI Cefazone OR Cefozon vial (500 mg) and (1.0 gm).
  RI Sulperazone 1500 vial (1000 mg + 500 mg sulbactam).
  RI Peractam 1500 vial (1000 mg + 500 mg sulbactam).
- **Ceftriaxone:** *RI Rocephin OR Longacef vial (500 mg) and (1.0 gm).*
  RI Ceftriaxone OR Triaxone vial (500 mg) and (1.0 gm).
  RI Cefotrix OR Cefaxone vial (250 mg), (500 mg) and (1.0 gm).

(Ceftriaxone is available in 2 forms, one for I.V and the other for I.M injection).

- **Ceftazidime:** *RI Fortum vial (250 mg) and (500 mg) and (1.0 gm).*
  RI Cefzim vial (500 mg) and (1.0 gm).
  RI Ceftazidime OR Kefadim vial (500 mg) and (1.0 gm).

Oral preparations of these drugs are not antipseudomonal or antistaphylococcal drugs and they are mainly used in otitis media, sinusitis and urinary tract infection. The dose is only **8 mg/kg/day** ... oral, given as a single daily dose (cefixime) or in 2 divided doses (cefpodoxime).

- **Cefixime:** *RI Suprax OR Ximacef suspension (100 mg/5 ml).*
  RI Suprax OR Ximacef capsules (200 mg).
- **Cefpodoxime:** *RI Orelox OR Cepodem suspension (40 mg/5 ml).*
  RI Orelox OR Cepodem tablets (100 mg).

D) Fourth-generation cephalosporins

These drugs have a more extended spectrum than that of third-generation, which includes resistant strains of enterobacter, citrobacter and acinebacter. Many of these organisms are relatively insensitive to drugs of third-generation cephalosporins. The dose is **50-100 mg/kg/day ... I.V**, divided into 2 doses.

- **Cefepime:** *RI Maxipime OR WinCef vial (500 mg) and (1.0 gm).*
- **Cefpirome:** *RI Cefrom vial (1.0 gm) and (2.0 gm).*

3. Aminoglycosides

Gentamicin:	5 - 7 mg/kg/day ... I.V. or I.M.
Tobramycin:	5 - 7 mg/kg/day ... I.V. or I.M.
Netilmicin:	5 - 7 mg/kg/day ... I.V. or I.M.
Amikacin:	15 - 20 mg/kg/day . I.V. or I.M.

The antibacterial activity of aminoglycosides is mainly against most aerobic gram-negative organisms including pseudomonas *(antigram-negative and anti-pseudomonal drugs)*. They are also active against staphylococci including penicillinase-producing organisms *(antistaphylococcal drugs)*. These drugs are poorly absorbed from the gut, so they are only used parenterally (I.M.or I.V).

Aminoglycosides are *serious drugs*. They are potentially *ototoxic* and *nephrotoxic*. Ototoxicity is irreversible and is both auditory (hearing) and vestibular (equilibrium). Nephrotoxicity is reversible and usually not severe, but the damage will be significant if aminoglycosides are given to patients with impaired renal function. Accordingly, 2 precautions are important:

1. The use of aminoglycosides should be *limited* to serious and life-threatening infections as neonatal septicemia, severe pneumonia and peritonitis. As they do not cross the blood-brain barrier, they should not be used in meningitis.

2. The recommended *dosage* should not be exceeded and renal function should be monitored especially if the treatment is extending for more than one week.

The differences between various drugs are mainly in their activity, toxicity and price.

* **Gentamicin** is the cheapest.

* **Tobramycin** seems to be the best for pseudomonal infections.

* **Amikacin** (Amikin) has the widest antibacterial activity, but it is more ototoxic than other drugs and is also the most expensive. Its use should be limited to gentamicin or tobramycin resistant infections.

*Gentamicin and amikacin are more nephrotoxic than tobramycin and netilmicin.

- **Gentamicin: 5 - 7 mg/kg/day ... I.V. or I.M.**

The daily dose is divided into 2 – 3 doses (every 8 – 12 hours).

* Available preparations are:

RI Garamycin pediatric amp. (20 mg/0.5 ml)
RI Gentamicin pediatric amp. (20 mg/0.5 ml).
RI Rigaminol pediatric amp. (20 mg/0.5 ml)

RI Garamycin amp. (40 mg/1 ml) and (80 mg/2 ml).
RI Gentamicin amp. (40 mg/1 ml) and (80 mg/2 ml).
RI Rigaminol amp. (40 mg/1 ml) and (80 mg/2 ml).
RI Refobacin amp. (40 mg/1 ml) and (80 mg/2 ml).
RI Epigent amp. (80 mg/2 ml).

- **Tobramycin: 5 - 7 mg/kg/day ... I.V. or I.M.**

  The daily dose is divided into 2 – 3 doses (every 8 – 12 hours).

  * Available preparations are:

  RI Nebcin OR Tobcin pediatric vial (20 mg/2 ml).
  RI Nebcin OR Tobcin adult vial (80 mg/2 ml).

- **Netilmicin: 5 - 7 mg/kg/day ... I.V. or I.M.**

  The daily dose is divided into 2 – 3 doses (every 8 – 12 hours).

  * Available preparations are:

  RI Netromycine vial (50 mg/2 ml) and (150 mg/2 ml).
  (Currently not available in Egypt)

- **Amikacin: 15 - 20 mg/kg/day ... I.V. or I.M.**

  The daily dose is divided into 2 doses (every 12 hours).

  * Available preparations are:

  RI Amikin pediatric vial (100 mg/2 ml).
  RI Amikacin pediatric vial (100 mg/2 ml).
  RI Amikin OR Amikacin vial (250 mg/2 ml).
  RI Amikin vial (500 mg/2 ml).

4. Macrolides

Erythromycin:	30 - 50 mg/kg/day ... oral (3 daily doses for 5 - 7 days).
Clarithromycin:	15 mg/kg/day ... oral (2 daily doses for 5 days).
Roxithromycin:	5 - 8 mg/kg/day ... oral (2 daily doses for 5 days).
Spiramycin:	150.000 - 300.000 IU/kg/day ... oral (2 daily doses for 5 days).
Azithromycin:	10 mg/kg/day ... oral (single daily dose for only 3 days).

- **Erythromycin: 30 - 50 mg/kg/day ... oral.**

  The daily dose is divided into 3 - 4 doses (every 6 - 8 hours).

The antibacterial spectrum is mainly against gram-positive organisms, so it is a good alternative to penicillin. Erythromycin is a **safe drug.** Mild gastric upset and diarrhea may occur. The main therapeutic indications are: (1) As a good alternative to penicillin in streptococcal pharyngitis, (2) Pyogenic skin infections, (3) It is the drug of choice for mycoplasma pneumonia, campylobacter gastroenteritis, pertussis and diphtheria. Available preparations are:

RI Erythrocin OR Erythrin suspension (200 mg/5 ml).
RI Erythromycin Pharco suspension (200 mg/5 ml).
RI Primomycin suspension (200 mg + 50 mg trimethoprim/5 ml).
RI Eryped suspension (400 mg/5 ml).
RI Erythrocin OR Erythrin tablets (250 mg) and (500 mg).

- **Clarithromycin: 15 mg /kg/day ... oral.**

The daily dose is divided into two equal doses. The drug has the same antibacterial spectrum of erythromycin.
* Available preparations are:

RI Klarimix suspension (125 mg/5 ml).
RI Klacid suspension (250 mg/5 ml).
RI Klacid OR Klarimix tablets (250 mg).
RI Klacid OR Klarimix tablets (500 mg).
RI Claribiotic capsules (250 mg) and (500 mg).

- **Roxithromycin: 5 - 8 mg/kg/day ... oral.**

The daily dose is divided into 2 doses (every 12 hours). The drug has the same antibacterial spectrum of erythromycin. It is only available in a tablets form.
* Available preparations are:

RI Roxicin tablets for children (150 mg).
RI Roxicin tablets (300 mg).
RI Roxid tablets (300 mg).

- **Spiramycin: 150.000 - 300.000 IU/kg/day ... oral or rectal.**

The daily dose is divided into 2 doses (every 12 hours). The drug has the same antibacterial spectrum of erythromycin. Available preparations are:

RI Rovamycin sachets (750.000 IU).
RI Rovamycin OR Rovac OR Spirex tablets (1.5 million IU).
RI Rovamycin OR Rovac OR Spirex tablets (3 million IU).

- **Azithromycin: 10 mg/kg/day ... oral.**

The daily dose is given as a single dose and the course of treatment is only 3 days. The drug has the advantages of less gastric upset, single daily dose, short course of treatment and better activity against H. influenza. The therapeutic level of the drug remains in the tissues for up to 10 days with the 3-day dosing regimen.
* Available preparations are:

RI Zisrocin OR Unitzithrin suspension (100 mg/5 ml)… 30 ml bottle.
RI Zithromax suspension 600 mg (200 mg/5 ml) … 15 ml bottle.
RI Zithromax suspension 900 mg (200 mg/5 ml) … 22.5 ml bottle.
RI Zithromax suspension 1200 mg (200 mg/5 ml) … 30 ml bottle.
RI Xithrone suspension (200 mg/5 ml) … 15 ml bottle.
RI Xithrone suspension (200 mg/5 ml) … 25 ml bottle.
RI Aziwok OR Azalide suspension (200 mg/5 ml) … 15 ml bottle.
RI Zithromax OR Xithrone capsules (250 mg).
RI Aziwok OR Azalide capsules (250 mg).
RI Zisrocin OR Zithrokan OR Xithrone capsules (500 mg).

5. Carbapenems

Imipenem:	60 - 100 mg/kg/day ... I.V. infusion or I.M.
Meropenem:	60 - 100 mg/kg/day ... I.V. or I.M.

The carbapenems, like all beta-lactams, penetrate the bacterial cell wall of susceptible organisms and inhibit cell wall synthesis. They are **broad-spectrum drugs** with activity against many gram-positive and gram-negative aerobic and anaerobic organisms. *Gram-positive activity* does not include penicillin-resistant bacterial strains (i.e. they are not antistaphylococcal drugs) while *gram-negative activity* includes pseudomonas aeruginosa (i.e. they are antipseudomonal drugs). *Anaerobic activity* includes Bacteroides, Peptostreptococcus, Clostridium, and Fusobacterium species.

These drugs can be used in empirical therapy of serious infections as septicemia, meningitis, and peritonitis. They are expensive drugs.

- **Imipenem: 60 - 100 mg/kg/day ... I.V. infusion or I.M**

The daily dose is divided into 3 doses (every 6-8 hours).

* Available preparations are:

RI Tienem vials (500 mg in 50 ml solution) ... for I.V infusion.
RI Tienem vials (500 mg)... for I.M injection.

- **Meropenem: 60 - 100 mg/kg/day ... I.V. or I.M.**

The daily dose is divided into 3 doses (every 8 hours).
The dose in bacterial meningitis is 120 mg/kg/day.

Meropenem is a newer drug of this group with antibacterial activity similar or better than imepenem. It can be used in serious abdominal infections and in bacterial meningitis in children above the age of 3 months.

* Available preparations are:

RI Meronem vials (500 mg).
RI Meronem vials (1.0 gm).

6. Other antibacterial drugs

Chloramphenicol:	50 - 100 mg/kg/day ... oral, I.V., I.M. or Rectal.
Co-trimoxazole:	4 mg + 20 mg/kg/day ... oral.
Aztreonam:	90 - 120 mg/kg/day ... I.V. or I.M.
Metronidazole:	7.5 mg/kg/dose ... I.V. ... every 8 hours.
Clindamycin:	20 - 40 mg/kg/day ... I.V.
Vancomycin:	40 - 80 mg/kg/day ... I.V.

• Chloramphenicol: 50 - 100 mg/kg/day... oral, I.V., I.M. or rectal.

The daily dose is divided into 3 - 4 doses (every 6 - 8 hours).

Chloramphenicol is a bacteriostatic drug that acts through interference with protein synthesis of microorganisms. The antibacterial activity is almost similar to that of ampicillin and co-trimoxazole, i.e. it is a **broad-spectrum drug.** It has the advantage of being very effective in salmonella infections. The concentration in CSF is remarkably high, so it is very effective in meningitis.

The major disadvantage of chloramphenicol is the rare possibility of fatal aplastic anemia. Although the risk rate is quite low (1 in 50.000 courses), the drug should not be used for simple infections. It also should be avoided in neonatal period as fatal shock-like state (Grey syndrome) may occur due to defective inactivation of the drug by the liver. The main indications are:

1. Bacterial meningitis (in combination with ampicillin).
2. Salmonella infection (typhoid fever or non-typhoidal salmonella infection).

RI Miphenicol OR Cidocetine vial (1.0 gm).
RI Miphenicol OR Cidocetine capsules (250 mg).
RI Miphenicol OR Cidocetine suspension (125 mg/5 ml).
RI Miphenicol OR Cidocetine supp. (125 mg).
RI Miphenicol OR Cidocetine supp. (250 mg).

It is also available with streptomycin, which acts as a local intestinal disinfectant in case of gastroenteritis.

RI Streptophenicol OR Streptocetine suspension (125 mg of each/5 ml).

• Co-trimoxazole: 4 mg + 20 mg/kg/day ... oral.

The daily dose is divided into 2 equal doses (every 12 hours). The dose may be doubled in severe infections.

Co-trimoxazole is a bacteriostatic combination of two drugs (trimethoprim and sulphamethoxazole in 1:5 ratio). At that ratio (1:5), the 2 drugs have a synergistic effect against most susceptible bacteria. The 2 drugs are antimetabolites as they block the metabolic events critical for the microorganisms. The antibacterial spectrum is similar to that of ampicillin and chloramphenicol. The drug is generally safe. Allergic skin rash may occasionally occur.

The main therapeutic indications are urinary tract infection, typhoid fever, shigella enteritis and otitis media. Each 5 ml of the suspension contains 40 mg trimethoprim and 200 mg sulphamethoxazole. Practical dosage is 1-2 teaspoon /10 kg/day in 2 divided doses every 12 hours.

RI Septrin suspension (40 mg + 200 mg/5 ml).
RI Sutrim OR Chemotrim suspension (40 mg + 200 mg/5 ml).
RI Septazole OR Supristol suspension (40 mg + 200 mg/5 ml).

All above trade name are also available as tablets for older children and adults. Each tablet contains 80 mg trimethoprim and 400 mg sulphamethoxazole.

- **Aztreonam: 90 - 120 mg/kg/day ... I.V. or I.M.**

The daily dose is divided into 2 - 3 doses (every 8 - 12 hours)
Aztreonam is the first drug of a new class of antibiotics known as monobactam. It is effective against a wide range of aerobic gram-negative organisms. Its activity is similar to that of third-generation cephalosporins.

* Available preparations are:

RI Azactam vials (500 mg) and (1.0 gm).

- **Metronidazole: 7.5 mg/kg/dose ... I.V. every 8 hours.**

Metronidazole infusion is used in treatment of serious anaerobic infections as in neonatal necrotizing enterocolitis, peritonitis and major abdominal surgery.

* Available preparations are:

RI Flagyl OR Elyzol infusion (500 mg/100 ml).

- **Clindamycin: 20 - 40 mg/kg/day ... I.V.**

The daily dose is divided into 2-3 doses (every 8-12 hours).
Clindamycin can be used in treatment of serious anaerobic infections instead of metronidazole. It is also useful in staphylococcal infections.

* Available preparation is:

RI Dalacin C amp. (300 mg).

- **Vancomycin: 40 - 60 mg/kg/day ... I.V.**

The daily dose is divided into 3 - 4 equal doses. The drug is considered as the drug of choice for resistant staphylococcal infection.
Available preparation is:

RI Vancocin vial (0.5 gm).

Oral antibacterial drugs

Narrow-spectrum drugs

Phenoxymethyl penicillin:	50.000 unit/kg/day (divided into 3-4 doses).
Cephalexin:	25 - 50 mg/kg/day (divided 3-4 doses).
Cephradine:	25 - 50 mg/kg/day (divided into 3-4 doses).
Cefadroxil:	25 - 50 mg/kg/day (divided into 2 doses).
Erythromycin:	30 - 50 mg/kg/day (divided into 3-4 doses).
Clarithromycin:	15 mg/kg/day (divided into 2 doses).
Roxithrormycin:	5 - 8 mg/kg/day (divided into 2 doses).
Spiramycin:	150.000 - 300.000 IU/kg/day (divided into 2 doses).
Azithromycin:	10 mg/kg/day (single daily dose).

Continued

Broad-spectrum drugs

Ampicillin or Sultamicillin:	50 - 100 mg/kg/day (divided into 3-4 doses).
* Amoxicillin or Co-amoxiclav:	25 - 50 mg/kg/day (divided into 3 doses).
Chloramphenicol:	50 - 100 mg/kg/day (divided into 3-4 doses).
Co-trimoxazole:	4 mg + 20 mg/kg/day (divided into 2 doses).
Cefuroxime:	20 - 40 mg/kg/day (divided into 2-3 doses).
Cefaclor:	20 - 40 mg/kg/day (divided into 2-3 doses).
Cefprozil:	20 - 40 mg/kg/day (divided into 2 doses).
Cefixime:	8 mg/kg/day (single daily dose).
Cefpodoxime:	8 mg/kg/day (divided into 2 doses).

Parenteral antibacterial drugs

Penicillins

Benzylpenicillin:	50.000 - 100.000 unit/kg/day (divided into 4 doses).
Cloxacillin:	50 - 100 mg/kg/day (divided into 4 doses).
Ampicillin or Sultamicillin:	50 - 100 mg/kg/day (divided Into 3-4 doses).
Amoxicillin or Co-amoxiclav:	50 - 100 mg/kg/day (divided into 3-4 doses).
Piperacillin:	200 - 300 mg/kg/day (divided into 3-4 doses).

Cephalosporins

Cephamandole:	50 - 100 mg/kg/day (divided into 2-3 doses).
Cefuroxime:	50 - 100 mg/kg/day (divided into 2-3 doses).
Cefotaxime:	50 - 100 mg/kg/day (divided into 2-3 doses).
Cefoperazone:	50 - 100 mg/kg/day (divided into 2-3 doses).
Ceftriaxone:	50 - 100 mg/kg/day (one daily injection).
Ceftazidime:	50 - 100 mg/kg/day (divided into 2 doses).
Cefepime:	50 - 100 mg/kg/day (divided into 2 doses).
Cefpirome:	50 - 100 mg/kg/day (divided into 2 doses).

Aminoglycosides

Gentamicin:	5 - 7 mg/kg/day (divided into 2-3 doses).
Tobramycin:	5 - 7 mg/kg/day (divided into 2-3 doses).
Netilmicin:	5 - 7 mg/kg/day (divided into 2-3 doses).
Amikacin:	15 - 20 mg/kg/day (divided into 2-3 doses).

Carpapenems

Imipenem:	60 - 100 mg/kg/day (divided into 3-4 doses ... I.V.).
Meropenem:	60 - 100 mg/kg/day (divided into 3-4 doses ... I.V.).

Other antibacterial drugs

Chloramphenicol:	50 - 100 mg/kg/day (divided into 3-4 doses).
Aztreonam:	90 - 120 mg/kg/day (divided into 2-3 doses).
Metronidazole:	7.5 mg/kg/dose ... (every 8 hours ... I.V. only).
Clindamycin:	20 - 40 mg/kg/day (divided in 2 doses ... I.V. only).
Vancomycin:	40 - 60 mg/kg/day (divided into 3-4 doses ... I.V.).

How to choose an antibiotic

Choice of the suitable antibacterial drug is usually based on the clinical diagnosis because the infective organism is usually the same. However, in serious infections, isolation of the organism by the appropriate culture is important and treatment is guided by the results of culture-sensitivity studies.

A) Antibiotics for simple infections

The use of ***one oral antibiotic*** is usually sufficient for the control of most simple infections. When an antibiotic is prescribed, a minimum course of ***five days*** should be used. Generally, the antibiotic should be used for 2 days after apparent cure to prevent relapse.

1. Streptococcal pharyngitis: One of three choices can be used:

- *Macrolides* as erythromycin, clarithromycin, roxithromycin, rovamycin or azithromycin.
- *First-generation cephalosporins* as cephalexin, cephradine or cefadroxil.
- *Phenoxymethylpenicillin* (Ospen).

Duration of therapy should be for, at least, 7 days.

2. Acute otitis media: As the organism is usually unknown, a broad-spectrum drug is usually needed. The 3 choices are:

- *Broad-spectrum penicillins* as ampicillin or amoxicillin. The newer drugs as sultamicillin (ampicillin + sulbactam) or co-amoxiclav (amoxicillin + clavulanic acid) are more effective than ampicillin or amoxicillin alone.
- *Second-generation cephalosporins* (as cefuroxime, cefaclor or cefprozil) or third-generation cephalosporins (as cefixime) are very effective.
- *New macrolides* as clarithromycin, roxithromycin or azithromycin can be also used.

3. Acute sinusitis: The same choices of acute otitis media can be applied.

4. Acute bacterial bronchitis: Again, the same choices of acute otitis media can be applied.

5. Skin pyoderma: Erythromycin or first-generation cephalosporins can be used. The new macrolides can be also used.

6. Urinary tract infection: Treatment should be guided by the results of culture-sensitivity studies. Several drugs are effective. Co-trimoxazole is the initial drug of choice. The same choices of acute otitis media can be also applied.

7. Acute infective enteritis (gastroenteritis): Antibiotic therapy is not indicated in the majority of cases, where correction of fluid and electrolyte balance is of prime importance. (See management of acute gastroenteritis).

8. Simple fever: In case of acute fever without localization (simple fever), evaluation of the general condition is extremely important for clinical differentiation between viremia, bacteremia and septicemia.

When the diagnosis of bacteremia is clinically made, broad-spectrum penicillin (as ampicillin or amoxicillin) can be used, especially when investigations for confirmation of bacterial origin are not available.

B) Antibiotics for serious infections

Serious infections as meningitis, pneumonia or septicemia necessitate urgent hospitalization and immediate ***parenteral combined antibiotic therapy.***

Investigations including appropriate cultures (CSF, blood or sputum culture) should be made. Duration of therapy should be for at least ***10 - 14 days.***

1. Bacterial meningitis: One of the third-generation cephalosporins as cefotaxime (200 mg/kg/day), ceftriaxone (100 mg/kg/day) or ceftazidime (100 mg/kg/day) is currently considered as the initial treatment of choice. Ampicillin (200 mg/kg/day...I.V.) may be added. The use of chloramphenicol in meningitis (100 - 200 mg/kg/day) should be limited to patients sensitive to cephalosporins.

2. Bacterial pneumonia: A combination of broad-spectrum penicillin (as ampicillin or amoxicillin) and an aminoglycoside (as gentamicin, tobramycin or amikacin) is an initial reasonable combination. In severe cases of bronchopneumonia, a third-generation cephalosporin as cefotaxime (100 mg/kg/day) can be added. In case of staphylococcal pneumonia, vancomycin (40 - 60 mg/kg/day, I.V., in 3-4 divided doses) should be added. The available preparation is *Vancocin vial (0.5 gm)*. When the possibility of pseudomonas infection is standing, anti-pseudomonal penicillin as piperacillin should be used.

3. Septicemia: An initial combination of ampicillin and an aminoglycoside is reasonable. Subsequent treatment should be guided by the result of blood culture and the clinical response.

4. Infective endocarditis: A combination of crystalline penicillin (300.000 unit/kg/day) and an aminoglycoside as gentamicin (5 - 7 mg/kg/day) is used. When the organism is not yet known, penicillinase-resistant penicillin as oxacillin or cloxacillin (200 mg/kg/day) should be also used. According to the clinical response and the results of blood cultures, antibiotics therapy can be modified. Therapy should be continued for, at least, 6 weeks to ensure complete organization of vegetations. Bed rest and treatment of congestive heart failure, if present, are also important.

5. Peritonitis: A combination of a third-generation cephalosporin (as cefotaxime) and an aminoglycoside (as amikacin) is an initial reasonable combination. Metronidazole (7.5 mg/kg/dose, I.V., every 8 hours) may be added to control anaerobic infections. Clindamycin, if available, can be used instead of metronidazole in a dose of 20 - 40 mg/kg/day... I.V., in 2 divided doses.

2. Antituberculous Drugs

First line drugs

Isoniazid (INH):	10 - 15 mg/kg/day ... oral.
Rifampicin or Rifampin (RIF):	10 - 20 mg/kg/day ... oral.
Pyrazinamide (PZA):	20 - 40 mg/kg/day ... oral.

Alternative drugs

Streptomycin (STM):	20 - 40 mg/kg/day ... I.M.
Ethambutol (ETM):	15 - 20 mg/kg/day ... oral.

Other drugs (Ethionamide, kanamycin, amikacin, para-aminosalicylic acid).

A) First line drugs

- **Isoniazid (INH): 10 - 15 mg/kg/day ... oral.**

It is given as a single daily dose. The total daily dose should not exceed 300 mg.

Isoniazid is the essential drug in tuberculosis. It can be given as a single drug (chemoprophylaxis) or in combination with other drugs (chemotherapy). Side effects as peripheral neuritis due to pyridoxine (vitamin B_6) deficiency are rare in children. Hepatic toxicity is also rare in patients without pre-existing liver disease.

* Available preparations are:

RI Isocid OR Inhibix tablets (50 mg).
RI Isocid forte tablets (200 mg).

- **Rifampicin or Rifampin (RIF): 10 - 20 mg/kg/day ... oral.**

It is given as a single daily dose, on an empty stomach, one hour before breakfast. Rifampicin is the most commonly used companion to isoniazid in double drug therapy of tuberculosis.

Side effects include discoloration of urine and saliva, gastric upset and hepatotoxicity. Periodic evaluation of liver function is important.

* Available preparations are syrups and capsules.

- **Syrups:** *RI Rimactane syrup (100 mg/5 ml).*
  RI Rifamox OR Rifam syrup (100 mg/5 ml).
  RI Rifadin OR Rifactine syrup (100 mg/5 ml).

- **Capsules:** *RI Rifampicin capsules (150 mg) and (300 mg).*
  RI Rifadin OR Rifampin capsules (150 mg) and (300 mg).
  RI Rimactane capsules (300 mg).

* **Both drugs (isoniazid + rifampicin)** are also available in one preparation.

RI Rimactazid OR Riozid tablets.

(Each tablet contains 150 mg isoniazid + 300 mg rifampicin).

RI Rimactazid pediatric tablets.

(Each tablet contains 60 mg isoniazid + 60 mg rifampicin).

- **Pyrazinamide: 20 - 40 mg/kg/day ... oral.**

It is given as a single daily dose.

Pyrazinamide can be used as a third drug (with isoniazid and rifampicin) during the first month or two of therapy in severe forms of tuberculosis as progressive primary pulmonary disease, miliary T.B. and T.B. meningitis (triple drug therapy). Its use can also shorten the duration of therapy to only 6 months.

Recent studies have shown that the drug is safe and well tolerated by children.

* Available preparations are:

RI Piraldina OR Pyrazinamide OR P.T.B tablets (500 mg).

* Recently, the **three first line drugs** (isoniazid + rifampicin + pyrazinamide) are available in one preparation.

RI Rimcure pediatric tablets.

(30 mg isoniazid + 60 mg rifampicin + 150 mg pyrazinamide).

RI Rimaster tablets.

(30 mg isoniazid + 150 mg rifampicin + 150 mg pyrazinamide).

RI Rimcure tablets.

(75 mg isoniazid + 150 mg rifampicin + 400 mg pyrazinamide).

B) Alternative drugs

- **Streptomycin: 20 - 40 mg/kg/day ... I.M.**

It is given as a single daily injection.

Streptomycin is an aminogycoside that was used as a third drug (with isoniazid and rifampicin) during the first month of therapy in severe forms of tuberculosis as locally progressive pulmonary disease, miliary T.B. and T.B. meningitis (Triple drug therapy). It is an ototoxic and nephrotoxic drug.

* Available preparation is:

RI Streptomycin vial (1.0 gm).

- **Ethambutol: 15 - 20 mg/kg/day ... oral.**

It is given as a single daily dose. Ethambutol is mainly used in older children and adults as an alternative to the expensive rifampicin. Reversible ocular complications may occur and include blurring of vision and colour blindness.

* Available preparations are:

RI Etibi tablets (500 mg).

Choice of antituberculous drugs

Treatment of tuberculosis with drugs should be combined (two or 3 drugs), continuous (given daily) and prolonged (for, at least, 6 - 9 months).

- **Double drug therapy:** It is the most commonly used regimen for all forms of tuberculosis. Isoniazid and rifampicin are the two standard drugs. After daily administration for 1 - 2 months, both drugs can be given daily or twice weekly for the remaining 7 - 8 months with equivalent results. In the twice-weekly regimen, the dose of isoniazid is doubled (20 - 30 mg/kg/dose) while the dose of rifampicin remains the same (15 - 20 mg/kg/dose). *The addition of pyrazinamide* during the first two months of therapy reduces the duration of treatment to only 6 months.

- **Triple drug therapy:** It is mainly used in severe forms of tuberculosis as miliary T.B., meningitis or locally progressive pulmonary disease. In this regimen, in addition to isoniazid and rifampicin, pyrazinamide is used for the first month or two of therapy. In areas where isoniazid resistance rate is high, a fourth drug (streptomycin, ethambutol or ethionamide) may be added. The duration of therapy in these severe forms should extend to 9 months or sometimes one year.

- **Single drug prophylaxis (INH prophylaxis):** Isoniazid chemoprophylaxis is used in children who are contacts to infectious cases or in children with tuberculin positive reaction without being vaccinated. Chemoprophylaxis may continue for 12 months.

Examples

1. A child, 6 years old (20 kg) with pulmonary tuberculosis.

Rl Isocid Forte tablets (200 mg).

One tablet every morning before breakfast.

Rl Rimactane OR Rifamox syrup (100 mg/ 5 ml).

Two teaspoons once daily, every morning.

(Treatment should be continued for at least 6-9 months).

2. An infant, one year old (8 kg) with pulmonary tuberculosis.

Rl Rimactazid pediatric tablets (60 mg + 60 mg).

Two tablets every morning before breakfast.

(Treatment should be continued for at least 6-9 months).

3. Antiviral Drugs

Acyclovir:	Treatment of herpes simplex and varicella-zoster infections.
Amantadine:	Treatment of influenza A virus infection.
Interferon alpha:	Treatment of chronic hepatitis B and chronic hepatitis C.
Famciclovir:	Treatment of acute herpes zoster.
Ganciclovir:	Treatment of cytomegalovirus infection.

- **Acyclovir: 10 mg/kg/dose ... I.V. (over 1 hour) or oral, every 8 hours.**

Duration of therapy is 7 - 10 days.

Acyclovir is an acyclic nucleoside with selective antiviral activity against herpes simplex and varicella-zoster virus by inhibition of viral DNA synthesis. The drug is mainly taken by the herpes virus-infected cells and therefore has potentially less toxicity for normal, uninfected host cells.

* *Parenteral form* is indicated in severe cases of herpes simplex as neonatal herpes simplex, herpes encephalitis and severe generalized herpes infections.
* *Oral forms* can be used in mild to moderate cases of herpes infections. They can be also used in chickenpox. As the drug is expensive, it should be only used when it is highly indicated. The drug is generally safe.
* Available preparations are:

RI Zovirax vial (250 mg/5 ml).
RI Zovirax OR Novirus suspension (200 mg/5 ml).
RI Zovirax OR Acyclovir tablets (200 mg) and (400 mg).
RI Novirus capsules (200 mg) and (400 mg).

- **Amantadine: 5-10 mg/kg/day ... oral.**

The daily dose is divided into 2 doses (every 12 hours). The total daily dose in children should not exceed 200 mg.

The drug is effective in prophylaxis and treatment of influenza A virus infection. It is also used in Parkinsonism. The drug is not expensive.
* Available preparations are:

RI Amantadine OR Amantine OR Adamine capsules. (100 mg).

Practical example

An infant, 10 months (10 kg) with severe herpes simplex infection.

RI Zovirax vial (250 mg/5 ml).
Add 2 ml (100 mg) to 60 ml saline and infuse over 1 hour
(20 drops/minute), every 8 hours for 10 days.

4. Antifungal Drugs

Nystatin:	100.000 unit/dose ... oral ... every 6 hours.
Miconazole:	30 - 60 mg/dose oral ... every 6 hours.
Fluconazole:	3 - 6 mg/kg/day ... oral or slow I.V. infusion.
Griseofulvin:	10 mg/kg/day ... oral.
Amphotericin B:	0.5 - 1.0 mg/kg/day ... slow I.V. infusion.

- **Nystatin: 100.000 unit/dose ... oral ... every 6 hours.**

The dose is fixed and not related to body weight. Treatment should be continued for, at least, 2 days after clinical cure. Average duration of therapy is 7 - 10 days.

Nystatin is a useful antifungal agent especially against candida albicans. It is used for oral moniliasis (Thrush) and gastrointestinal monilial infection. The drug acts locally and is not absorbed into the systemic circulation, so it is not useful in systemic fungal infection. Side effects are minimal. Diarrhea may occur.

* Available preparations are:

RI Mycostatin OR Fungistatin drops (100.000 unit/ml).
RI Nystatin OR Antimycot drops (100.000 unit/ml).

Practical dosage is one ml (one dropper) every 6 hours for 7 - 10 days.

- **Miconazole: 30 mg/dose ... oral ... every 6 hours (for infants).**
  60 mg/dose ... oral ... every 6 hours (for children).

Miconazole is a synthetic antifungal drug, which is useful for treatment of oral moniliasis and gastrointestinal monilial infection. It may also have an anti-bacterial activity against gram-positive infections. Like nystatin, it acts locally.

The drug should not be swallowed immediately but it is better to be left in the mouth as long as possible. Treatment is continued for several days after clinical cure. Available preparations are:

RI Daktarin oral gel 2% (120 mg/spoon).
RI Miconaz OR Micazole oral gel 2% (120 mg/spoon).
RI Micoban oral gel 2% (120 mg + 30 mg Lidocaine /spoon).

Practical dosage is 1/4 spoon (for infants) and 1/2 spoon (for children), every 6 hours for 7 - 10 days.

- **Fluconazole: 3 - 6 mg/kg/day ... oral or slow I.V.**

The daily dose is given as a single dose or divided every 12 hours. In serious systemic infections, the dose may be increased to 12 mg/kg/day.

Fluconazole is a synthetic broad-spectrum antifungal drug, which is effective in mucosal, cutaneous and systemic fungal infections. Oral forms are indicated in oropharyngeal candidiasis and in cutaneous fungal infections as tinea pedis, tinea

corporis and candida infection. Duration of therapy is usually 1-3 weeks. Parenteral form is reserved to serious systemic fungal infections as candidemia and candida infection of the lungs, peritoneum, endocardium or urinary tract. Duration of therapy depends on the clinical and laboratory response and it can extend for several weeks.

The drug is generally safe but dose adjustment should be made in prematures and in patients with renal impairment.

* Available preparations are:

RI Diflucan syrup (25 mg/5 ml).
RI Diflucan OR Triconal OR Alkanazol capsules (50 mg).
RI Diflucan OR Triconal OR Alkanazol capsules (150 mg).
RI Diflucan I.V. infusion (100 mg/50 ml).

- **Griseofulvin: 10 mg/kg/day ... oral.**

The daily dose is divided into 2-3 doses. Therapy is for at least, 4 - 6 weeks.

Griseofulvin is an antifungal agent, useful for treatment of deep-seated mycotic infections of the hair, nails and skin. It is especially useful for treatment of fungal infections of the scalp (ring worm and favus). For tinea capitis (favus), treatment is necessary for 8 - 12 weeks. Side effects may include gastrointestinal disturbance and allergic reactions.

* Available preparations are:

RI Ultragrisofulvin suspension (125 mg/5 ml).
RI Ultragrisofulvin tablets (125 mg).

- **Amphotericin B: 0.5 - 1.0 mg/kg/day ... slow I.V. infusion.**

Treatment should start with low dosage and the dose is gradually increased until the full therapeutic dose is achieved, then, the drug can be given every other day or even twice per week. Therapy is usually continued for several weeks or months and until clinical and laboratory improvement becomes evident.

Amphotericin B is a systemic fungicidal drug effective against deep-seated fungal infections as disseminated histoplasmosis or cocidioidomycosis. It is only indicated in progressive potentially fatal systemic fungal infections.

Amphotericin B is a serious drug with several side effects. Anaphylaxis, convulsions, generalized pain and thrombocytopenia are serious complications.

* Available preparation is:

RI Fungizone vial (50 mg/20 ml).

(The contents of the vial are added to 500 ml glucose 5% to make a colloidal suspension with the concentration of 0.1 mg/ml. Practical dosage is 5 - 10 ml/kg, given by slow I.V. infusion over 1 - 2 hours. The bottle should be protected from light and all other drugs and electrolytes should not be added to the suspension).

5. Antiprotozoal Drugs

Drugs for amoebiasis (Amoebicidal drugs)	
Metronidazole:	50 mg/kg/day ... oral ... for 10 days.
Diloxanide furoate:	10 mg/kg/day ... oral ... for 10 days.
Tinidazole:	50 mg/kg ... oral ... single dose.
Secnidazole:	50 mg/kg ... oral ... single dose.
Drugs for giardiasis	
Metronidazole:	25 mg/kg/day ... oral ... for 7 days.
Furazolidone:	8 mg/kg/day ... oral ... for 10 days.
Drugs for malaria	
Chloroquine:	10 mg/kg (initial), then 5 mg/kg/day ... for 3 days.
Pyrimethamine:	1 mg/kg ... oral ... single dose.

A) Amoebicidal drugs

- **Metronidazole: 50 mg/kg/day ... oral ... for 10 days.**

The daily dose is divided into 3 equal doses.
Metronidazole is a **tissue amoebicidal drug**, used for treatment of acute invasive amoebiasis of intestine (vegetative form), liver or other organs. The drug is also effective against chronic luminal cases (cyst passers), but it is not the drug of choice. The main side effects are nausea, diarrhea and metallic taste.
* Available preparations are:

RI Flagyl OR Amrizole suspension (125 mg/5 ml).
RI Metrozole OR Dumozol suspension (125 mg/5 ml).
RI Flagyl OR Amrizole OR Metrozole tablets (250 mg).
RI Flagyl OR Amrizole OR Dumozol tablets (500 mg).

- **Metronidazole (infusion): 7.5 mg/kg/dose ... every 8 hours.**

It is used in amoebic hepatitis or amoebic liver abscess.
It is also used in peritonitis and some cases of lung abscess to act against the anaerobic bacterial infections.

RI Flagyl infusion (500 mg/100 ml).
RI Flazol infusion (500 mg/100 ml).
RI Dumozol infusion (500 mg/100 ml).

- **Diloxanide furoate: 10 mg/kg/day ... oral ... for 10 days.**

The daily dose is divided into 2 equal doses.
Diloxanide furoate is a **luminal amoebicidal drug**, used for treatment of asymptomatic cyst passers. It is important to remember that eradication of these

cysts is important because it is the infective form of amoebiasis, while the trophozoite form is non-infective.

The drug is safe, but it is better to be avoided below the age of 2 years.

* Available preparations are:

R/ Furamide tablets (500 mg).
R/ Farcomid tablets (500 mg).

* It is also available in combination with metronidazole:

RI Furazol suspension (100 mg diloxanide + 200 mg metronidazole/5 ml).
RI Dilozole suspension (100 mg diloxanide + 200 mg metronidazole /5 ml).
RI Dimetrol suspension (100 mg diloxanide + 200 mg metronidazole/ 5 ml).
RI Furazol tablets (250 mg diloxanide + 200 mg metronidazole).
RI Dilozole tablets (250 mg diloxanide + 200 mg metronidazole).
RI Dimetrol tablets (250 mg diloxanide + 200 mg metronidazole).

With the suspension form, the daily dose is one teaspoon per 10 kg body weight and with the tablet form the dose is 1 tablet for each 25 kg body weight.

- **Tinidazole: 50 mg/kg ... oral ... single dose.**

It has the advantage of single dosage but it is not available in syrup form.

* It is only available as tablets.

RI Fasigyn tablets (500 mg).
RI Protozole tablets (500 mg).

(Practical dosage is one tablet for each 15 kg body weight).

- **Secnidazole: 50 mg/kg ... oral ... single dose.**

It is similar to tinidazole.

* Available preparations are:

RI Fladazole Sachets (500 mg).
RI Fladazole OR Flagentyl OR Eurozole tablets (500 mg).

(Practical dosage is one sachet or tablet for each 15 kg body weight).

B) Drugs for giardiasis

- **Metronidazole: 25 mg/kg/day ... oral ... for 7 days.**

The daily dose is divided into 3 doses.

* It is available as suspension (125 mg/5 ml) and tablets (250 mg).

RI Flagyl OR Amrizole suspension (125 mg/5 ml).
RI Metrozole OR Dumozol suspension (125 mg/5 ml).
RI Flagyl OR Amrizole OR Metrozole tablets (250 mg).
RI Flagyl OR Amrizole OR Dumozol tablets (500 mg).

- **Furazolidone: 8 mg/kg/day ... oral ... for 10 days.**

The daily dose is divided into 3 - 4 doses.

The drug is also effective against campylobacter enteritis and, to some extent, against salmonella, shigella and E. coli enteritis.

The drug is contraindicated in patients with G6PD deficiency.

* Available preparations are:

RI Fudizol suspension (16.6 mg/5 ml).
RI Furakin tablets (50 mg).

C) Drugs for malaria

- **Chloroquine phosphate: 3 days treatment ... oral.**

- Day 1: Initial dose: 10 mg base/kg.
After 6 hours: 5 mg base/kg.
- Day 2: one dose: 5 mg base/kg.
- Day 3: one dose: 5 mg base/kg.

It kills the erythrocyte forms of malaria at all stages of development and gives radical cure.

* Available preparations are:

RI Chloroquine syrup (80 mg/5 ml).
RI Chloroquine tablets (150 mg base).
RI Alexoquine tablets (150 mg base).

- **Chloroquine (infusion): 5 mg base/kg ... I.V. ... initial dose, to be repeated after 6 hours.**

The calculated dose is added to saline (10 ml/kg) and infused I.V. over 3 hours. A second dose is given after 6 hours.

It is indicated in severe cases as an initial therapy (in the first day) when oral intake cannot be tolerated. Treatment is continued orally in the second and third days.

* Available preparation is:

RI Chloroquine phosphate amp. (150 mg base/5 ml).
(Each 1.0 ml contains 30 mg base).

- **Pyrimethamine: 1 mg/kg ... oral ... single dose.**

It is used to destroy gametocytes and thus to protect the community if mosquitoes are present. It is also useful in treatment of toxoplasmosis.

*Available preparation is:

RI Daraprim tablets (25 mg).

6. Antihelmintic Drugs

Drugs for nematodes (Round worms)

Albendazole:	100 mg/dose ... oral ... twice daily ... for 3 days.
Flubendazole:	100 mg/dose ... oral ... twice daily ... for 3 days.
Mebendazole:	100 mg/dose ... oral ... twice daily ... for 3 days.

Drugs for cestodes (Tape worms)

Niclosamide:	1.0 gram ... oral ... single dose.
Praziquentel:	5 - 10 mg/kg ... oral ... single dose.
Flubendazole:	100 mg/dose ... oral ... twice daily ... for 3 days.

Drugs for trematodes (Antibilharzial drugs)

Praziquentel:	40 - 60 mg/kg ... oral ... single dose.

A) Drugs for nematodes

These drugs are used for treatment of ascaris, ankylostoma (hook worms), oxyuris (pin worms), Strongyloides and trichuris.

- **Albendazole: 100 mg/dose ... oral ... twice daily ... for 3 days.**

The dose for adults is 200 mg.

The drug is effective against all nematodes. For treatment of oxyuris, one single dose (100 mg) is sufficient. The drug is also effective against cestodes (tapeworms). It is generally a safe drug with no side effects.

* Available preparations are:

RI Alzental OR Bendax OR Vermizole suspension (100 mg/5 ml).
RI Alzental OR Bendax OR Vermizole tablets (200 mg).

- **Flubendazole: 100 mg/dose ... oral ... twice daily ... for 3 days.**

The dose (100 mg) is the same for all ages.

Flubendazole is effective against all nematodes. For oxyuris, one single dose (100 mg) is sufficient. The drug is also effective against cestodes (tape worms). It is generally a safe drug with no side effects.

* Available preparations are:

RI Fluvermal OR Fluver OR Verm -All suspension (100 mg/5 ml).
RI Fluvermal OR Fluver OR Verm-All tablets (100 mg).

- **Mebendazole: 100 mg/dose ... oral ... twice daily ... for 3 days.**

The dose (100 mg) is the same for all ages. The drug is as effective as flubendazole. Available preparations are:

RI Antiver OR Vermin OR Anthelmin suspension (100 mg/5 ml).
RI Antiver OR Vermin OR Mebamox tablets (100 mg).

B) Drugs for cestodes

These drugs are used for treatment of taenia saginata, taenia solium, hymenolepis nana and diphyllobothrium latum.

- **Niclosamide: 1.0 gram ... oral ... single dose.**

The dose is increased to 1.5 gm in children above the age of 10 years.

It is effective against all cestodes. In case of hymenolepis nana, the daily dose is continued for 6 days.

* Available preparations are:

RI Yomesan tablets (500 mg).
RI Niclosan tablets (500 mg).

(The tablets should be thoroughly chewed after a light meal).

- **Praziquentel: 5 - 10 mg/kg ... oral ... single dose.**

The drug is effective against all cestodes.

In case of hymenolepis nana, the dose should be increased to 25 mg/kg (single dose). In case of cysticercosis, the dose is increased to 50 mg/kg and it is given daily (in 3 divided doses) for 14 days.

* Available preparations are:

RI Epiquantel suspension (600 mg/5 ml).
RI Praziquentel tablets (600 mg).
RI Distocide tablets (600 mg).
RI Biltricide tablets (600 mg).

- **Albendazole: 100 - 200 mg/dose ... twice daily ... for 3 days.**
- **Flubendazole: 100 mg/dose ... twice daily ... for 3 days.**

(See above)

C) Antibilharzial drugs

- **Praziquentel: 40 - 60 mg/kg ... oral ... single dose.**

It is the drug of choice for all types of bilharziasis.

* Available preparations are:

RI Epiquantel suspension (600 mg/5 ml).
RI Praziquentel tablets (600 mg).
RI Distocide tablets (600 mg).
RI Biltricide tablets (600 mg).

2

Antipyretics and Anti-inflammatory Drugs

1. Antipyretics.
2. Nonsteroidal Anti-inflammatory Drugs.
3. Corticosteroids.

1. Antipyretic Drugs

Eight drugs are available as antipyretic agents in pediatric practice:

Acetaminophen (Paracetamol):	10 - 15 mg/kg/dose ... oral or rectal.
Ibuprofen (Brufen):	10 - 15 mg/kg/dose ... oral or rectal.
Acetylsalicylic acid (Aspirin):	10 - 15 mg/kg/dose ... oral, rectal or I.V.
Metamizole (Novalgin):	10 - 15 mg/kg/dose ... oral or rectal.
Mefenamic acid (Ponstan):	5 mg/kg/dose ... oral.
Diclofenac (Voltaren):	0.5 - 1.0 mg/kg/dose ... oral or rectal.
Ketoprofen (Ketofan):	0.5 - 1.0 mg/kg/dose ... oral.
Nimesulide (Sulide)	2 - 3 mg/kg/dose ... oral.

Mechanism of action

Antipyretic drugs produce their effect through inhibition of prostaglandin-E synthesis. Prostaglandin-E plays an essential role in pathogenesis of fever as it causes upward deviation of the hypothalamic heat regulation center. The associated analgesic effect is probably through blocking the synapses of the spinothalamic tracts in the thalamus, thus blocking the painful stimuli.

- **Paracetamol: 10 - 15 mg/kg/dose ... oral or rectal.**

The dose can be repeated every 4 - 6 hours.

Paracetamol is by far the most commonly used antipyretic drug in pediatric practice. It is generally a safe drug. However, accidental overdosage may lead to hepatic necrosis. Toxic serum level is 300 mcg/ml. It is available as:

1. Drops (for infants)

RI Pyral OR Cetal OR Pyremol drops (100 mg/ml = 5 mg/drop).
RI Tempra drops (80 mg/0. 8 ml = 5 mg/drop).
(Practical dosage is 2 drops/kg/dose).

2. Syrups and tablets (for children)

RI Pyral OR Paramol OR Paracetamol OR Cetamol syrup (120 mg/5 ml).
RI Abimol syrup (150 mg/5 ml) OR Tempra syrup (160 mg/5 ml).
RI Fevano syrup (200 mg/5 ml).
RI Cetal OR Temporal suspension (250 mg/5 ml).
RI Pyral OR Cetal OR Abimol OR Paramol OR Pyremol tablets (500 mg).

3. Pediatric suppositories (when oral intake is difficult e.g. vomiting)

RI Paramol infantile supp. (125 mg).
RI Paralex infantile supp. (160 mg).
RI Sedamol pediatric supp. (200 mg).
RI Pyral pediatric supp. (250 mg).
RI Abimol OR Pyremol pediatric supp. (300 mg).

(Obviously, choice of the suitable syrup or suppository depends on the weight).

* **Ibuprofen: 10 - 15 mg/kg/dose ... oral or rectal.**

The dose can be repeated every 6 - 8 hours.

* It is available as syrup, tablets and suppositories.

RI Brufen OR Marcofen OR Profinal syrup (100 mg/5 ml).
RI Ultrafen OR Ibufen syrup (100 mg/5 ml).
RI Marcofen infantile supp. (100 mg).
RI Ultrafen pediatric supp. (200 mg).
RI Marcofen pediatric supp. (300 mg).
RI Brufen OR Ultrafen OR Ibufen OR Profinal tablets (200 mg).
RI Brufen OR Marcofen OR Ultrafen OR Profinal tablets (400 mg).
RI Brufen OR Marcofen OR Ultrafen adult supp. (500 mg).
RI Brufen OR Ultrafen OR Profinal tablets (600 mg).

* It is also available in combination with paracetamol:

RI Megafen syrup (100 mg ibuprofen +162.5 mg paracetamol /5 ml).
RI Cetafen syrup (100 mg ibuprofen +162.5 mg paracetamol /5 ml).
RI Megafen OR Cetafen Tablets (200 mg ibuprofen + 325 mg paracetamol).

* **Acetylsalicylic acid: 10 - 15 mg/kg/dose ... oral, rectal or I.V or I.M.**

The dose can be repeated every 4 - 6 hours.

The drug is not available in a syrup form suitable for children. Gastric upset and vomiting may follow its intake on an empty stomach.

The drug should be avoided in infants (metabolic disturbance) and in patients with G6PD deficiency (acute hemolysis).

* Available preparations are:

1. **Infantile soluble (chewable) tablets:** For children 2 - 6 years.

   RI Aspocid infantile tablets (75 mg).
   RI Alexoprine OR Rivo infantile tablets (75 mg).

2. **Infantile suppositories:** When oral intake is difficult.

   RI Vegaskine infantile supp. (150 mg + 10 mg phenobarbital).
   RI Rivo infantile supp. (162 mg).

3. **Standard tablets:** For older children above 6 years (300 mg and 500 mg).

   RI Alkasprine OR Alexoprine tablets (300 mg).
   RI Aspeol OR Aspirin tablets (500 mg).

4. **Vials:** For I.M. or I.V. injection.
   It is used in hyperpyrexia (temperature above 41.00 °C). It is generally safe.

   RI Aspegic injectable (500 mg/5 ml).
   (Practical dosage 1 ml /10 kg/dose (. I.V. or I.M.).

- **Metamizole: 10 - 15 mg/kg/dose ... oral or rectal.**

The dose can be repeated every 6 - 8 hours.
Metamizole is one of the pyrazolone derivatives. It is a highly effective antipyretic and analgesic drug. It is a serious drug and fatal agranulocytosis may occasionally occur. When other drugs are available, it should be avoided.
* Available preparations are:

RI Novalgin OR Novacid syrup (250 mg/5 ml).
RI Novalgin OR Novacid pediatric supp. (300 mg).
RI Novalgin OR Novacid OR Analgin tablets (500 mg).
RI Novalgin OR Novacid adult supp. (500 mg).

- **Mefenamic acid: 5 mg/kg/dose ... oral.**

The dose can be repeated every 6 - 8 hours.
* It is available as oral suspension and capsules.

RI Ponstan suspension (50 mg/5 ml).
RI Ponstan OR Farostan OR Mefentan OR Pono capsules (250 mg).

- **Diclofenac: 0.5 - 1.0 mg/kg/dose ... oral or rectal.**

The dose can be repeated every 6 – 8 hours.
* It is available as oral drops, pediatric suppositories and tablets.

RI Cataflam OR Dolphin-K drops (0.5 mg/drop).
RI Voltaren OR Dolphin OR Baby relief pediatric supp. (12.5 mg).
RI Voltaren OR Dolphin OR Baby relief pediatric supp. (25 mg).
RI Voltaren OR Cataflam OR Antiflam OR Rapiflam tablets (25 mg).
RI Voltaren OR Cataflam OR Antiflam OR Rapiflam tablets (50 mg).

- **Ketoprofen: 0.5 - 1.0 mg/kg/dose ... oral.**

The dose can be repeated every 6 - 8 hours.
* It is available as oral suspension and tablets.

RI Ketofan suspension (12.5 mg/5 ml).
RI Ketofan OR Ketolgin OR Alcofan tablets (25 mg).
RI Ketofan OR Ketolgin OR Alcofan tablets (50 mg).

- **Nimesulide: 2 - 3 mg/kg/dose ... oral.**

The dose can be repeated every 6 - 8 hours.
* It is available as oral suspension and tablets.

RI Sulide OR Nimalox OR Nilsid OR Mesulan suspension (50 mg/5 ml).
RI Sulide OR Nimalox OR Nilsid OR Mesulide Tablets (100 mg).

*** Notice**

- Paracetamol and ibuprofen are safe and should be the first choice in children.
- Acetylsalicylic acid is the only one available in a safe parenteral form that can be used in case of hyperpyrexia.

2. Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Salicylic acid derivatives

Acetylsalicylic acid (Aspirin): 80 - 100 mg/kg/day ... oral.

Propionic acid derivatives

Ibuprofen:	30 - 50 mg/kg/day ... oral.
Ketoprofen:	1 - 3 mg/kg/day ... oral.
Naproxen:	10 - 20 mg/kg/day ... oral or rectal.

Acetic acid derivatives

Diclofenac:	1 - 3 mg/kg/day ... oral.
Aceclofenac:	2 - 6 mg/kg/day ... oral.
Indomethacin:	1 - 3 mg/kg/day ... oral.
Tolmetin:	20 - 30 mg/kg/day ... oral.

Oxicam derivatives

Piroxicam:	0.5 - 1.0 mg/kg/day ... oral or rectal
Meloxicam	0.2 – 0.5 mg/kg/day... oral or rectal.

Mechanism of action and therapeutic indications

The mechanism of action of all these drugs is essentially the same. They inhibit prostaglandin synthesis by blocking the conversion of arachidonic acid into different chemical mediators. Prostaglandins play an important role in inflammation. Prostaglandin F is responsible for erythema, oedema, pain and fever. So, these drugs are analgesic, antipyretic and anti-inflammatory drugs.

Rheumatoid arthritis is by far the commonest indication for chronic use of these drugs. It is important to remember that therapeutic response may take as long as 6 - 8 weeks. Acetylsalicylic acid, naproxen, diclofenac and ibuprofen are the most commonly used drugs in children. The main side effect of all these drugs is gastric upset, so they should be given after meals.

- **Acetylsalicylic acid: 80 - 100 mg/kg/day ... oral.**

The daily dose is divided into 3 equal doses (after meals).

RI Alkasprine OR Alexoprine forte OR Aspocid tablets (300 mg).
RI Aspeol OR Aspirin OR Rhonal tablets (500 mg).

- **Ibuprofen: 30 - 50 mg/kg/day ... oral.**

The daily dose is divided into 3 equal doses (after meals).
The drug is probably as effective as acetylsalicylic acid.

RI Brufen OR Marcofen OR Ultrafen OR Ibufen syrup (100 mg/5 ml).
RI Brufen OR Ultrafen OR Ibufen tablets (200 mg).
RI Brufen OR Ultrafen OR Prifinal tablets (400 mg) and (600 mg).

- **Ketoprofen: 1 - 3 mg/kg/day ... oral.**

  The daily dose is divided into 3 equal doses (after meals).

  RI Ketofan suspension (12.5 mg/5 ml).
  RI Ketofan OR Ketolgin OR Alcofan tablets (25 mg) and (50 mg).

- **Naproxen: 10 - 20 mg/kg/day ... oral or rectal.**

  The daily dose is divided into 2 equal doses (morning and evening). Naproxen has the advantage of being given only twice daily.

  RI Naprosyn OR Naprofen OR Naprogesic tablets (250 mg).
  RI Naprosyn OR Naprofen OR Naprogesic tablets (500 mg).
  RI Naprosyn OR Naprogesic adult supp. (500 mg).

- **Diclofenac: 1 - 3 mg/kg/day ... oral.**

  The daily dose is divided into 2 - 3 doses. Recent studies have proved that the drug is highly effective and safe.

  RI Voltaren OR Cataflam OR Antiflam OR Rapiflam tablets (25 mg).
  RI Voltaren OR Cataflam OR Antiflam OR Rapiflam tablets (50 mg).
  RI Voltaren OR Rheumafen S-R tablets (75 mg) and (100 mg).

- **Aceclofenac: 2 - 6 mg/kg/day ... oral.**

  The daily dose is divided into 2 - 3 doses.

  RI Bristaflam OR Amoflam OR Fenac tablets (100 mg).

- **Indomethacin: 1 - 3 mg/kg/day ... oral.**

  The daily dose is divided into 3 equal doses.
  Dyspeptic symptoms and headache are the main side effects.

  RI Indocid OR Indomethacin capsules (25 mg) and (50 mg).

- **Tolmetin: 20-30 mg/kg/day ... oral.**

  The daily dose is divided into 2-3 equal doses.
  Dyspeptic symptoms and headache are the main side effects.

  RI Tolectin OR Rumatol capsules (200mg).
  RI Tolectin OR Rumatol capsules (400 mg).

- **Piroxicam: 0.5 - 1.0 mg/kg/day ... oral or rectal.**

  The drug is given as a single daily dose.

  RI Felden OR Dispercam capsules (10 mg) and (20 mg).
  RI Felden OR Dispercam suppositories (20 mg).

- **Meloxicam: 0.2 - 0.5 mg/kg/day ... oral or rectal.**

  The drug is given as a single daily dose.

  RI Mobic OR Melocam OR Mexicam tablets (7.5 mg) and (15 mg).
  RI Mobic OR Melocam OR Mobitil suppositories (15 mg).

3. Corticosteroids

Short-acting drugs (Duration for 4-6 hours)	Long-acting drugs (Duration for 8-12 hours)	Inhalation or surface-active drugs
Hydrocortisone	Dexamethasone	Beclomethasone
Prednisone	Betamethasone	Budesinide
Prednisolone		Fluticasone

Parenteral corticosteroids

Hydrocortisone:	5.0 - 10 mg/kg/dose ...	I.V. or I.M ... every 6 hours.
Methylprednisolone:	0.5 - 1.0 mg/kg/dose ...	I.V. or I.M ... every 6 hours.
Dexamethasone:	0.25 - 0.5 mg/kg/dose ...	I.V. or I.M ... every 12 hours.

Oral corticosteroids

Hydrocortisone: 2 mg/kg/day.
Prednisone or prednisolone: 2 mg/kg/day.
Dexamethasone or betamethasone: 0.1 - 0.2 mg/kg/day.

Inhalation corticosteroids

Beclomethasone:	100 mcg/dose ... 3 times daily.
Budesinide:	100 - 200 mcg/dose ... 2 times daily.
Fluticasone:	50 -100 mcg/dose ... 2 times daily.

Mechanism of action

Corticosteroids are potent anti-inflammatory drugs. They produce their effect through different mechanisms:

1. Inhibition of prostaglandin synthesis through inhibition of arachidonic acid formation. They also prevent the release of the already formed chemical mediators. It is important to note that the mechanism is different from that of nonsteroidal anti-inflammatory drugs. In other words, formation and release of prostaglandins is made through 3 steps:

(a) Formation of arachidonic acid from phospholipids.
(b) Formation of prostaglandins from arachidonic acid.
(c) Release of the already formed prostaglandins.

- Corticosteroids inhibit steps a and c.
- Nonsteroidal anti-inflammatory drugs inhibit step b.

2. Inhibition of leukocyte migration.
3. Inhibition of interleukin formation by monocytes.
4. Increased synthesis of beta-adrenergic receptors with the resultant increase in catecholamine activity.

Relative potency of different drugs

Hydrocortisone and aldosterone are the two principal hormones normally produced by the adrenal cortex. **Hydrocortisone** (cortisol) has a glucocorticoid (anti-inflammatory) and mineralocorticoid (salt retaining) effects. Several drugs have been synthesized with "hydrocortisone-like activity". The relative potency of these synthetic drugs in relation to hydrocortisone is as follow:

Prednisone and **prednisolone:** The anti-inflammatory effect is 5 times as that of hydrocortisone, while the sodium retaining effect is slightly less than that of hydrocortisone (about 0.8).

Dexamethasone and **betamethasone:** The anti-inflammatory effect is 50 times as that of hydrocortisone, while the sodium retaining effect is negligible.

In other words, the pharmacological effect of 10 mg hydrocortisone is equivalent to 2 mg prednisone or prednisolone and to 0.2 mg dexamethasone or betamethasone.

Indications of corticosteroid therapy

Corticosteroids are used in a large variety of apparently unrelated conditions. However, indications can be classified into 3 main groups:

1. Replacement therapy: Where physiological low doses of hydrocortisone (2 mg/kg/day) are used in chronic adrenocortical insufficiency.

2. Pharmacotherapy: Where large doses, far beyond the physiological requirements, are used for therapeutic purposes. Hydrocortisone or other synthetic steroids are used for this purpose. The main indications are:

(a) Emergencies:
- Severe acute asthma: Hydrocortisone or methylprednisolone.
- Increased intracranial pressure: Dexamethasone.
- Severe allergy: Hydrocortisone or Dexamethasone.

(b) Chronic inflammatory conditions: Rheumatic diseases (rheumatic carditis, systemic form of juvenile rheumatoid arthritis, systemic lupus erythematosus and dermatomyositis), chronic active hepatitis and ulcerative colitis.

(c) Neurological inflammatory conditions as infectious polyneuritis and transverse myelitis.

(d) Renal conditions as nephrotic syndrome and chronic glomerular diseases.

(e) Hematological conditions as idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, aplastic and hypoplastic anemia.

(f) Persistent asthma: Oral or inhalation steroids can be used.

(g) Malignancies as acute leukemia and lymphoma.

3. Immunosuppression: following organ transplantation as in renal and hepatic transplantation.

Side effects of prolonged steroid therapy

Short-term use of steroids (for days or a week) has no side effects. Prolonged use in pharmacologic doses has many side effects:

1. Growth retardation especially in growing children.
2. Cushing's syndrome (moon face, hirsutism, acne, stria and hypertension).
3. Wasting of muscles and osteoporosis of bones.
4. Salt retention (oedema, weight gain) and hypokalemia.
5. Flaring of infections (bacterial, viral or tuberculous).
6. Sudden withdrawal, after prolonged use, leads to acute adrenal failure.

Precautions during prolonged steroid therapy

1. High protein diet and calcium supplementation are important to prevent muscle wasting and osteoporosis.
2. Fresh orange juice or potassium syrup should be given daily to prevent hypokalemia (see mineral therapy).
3. Infections should be diagnosed early and treated adequately.
4. Periodic monitoring of blood pressure, weight and length is important.
5. Sudden withdrawal should be avoided. **Gradual tapering** of the dose over few weeks is important.

Side effects of prolonged steroid therapy can be largely minimized by the **"alternate-day therapy"**, where the calculated daily dose is given as a single dose at 6 - 8 a.m. every other day (every other morning therapy).

A) Parenteral corticosteroids

Parenteral preparations are used in acute life-threatening conditions as acute severe asthma, severe allergy (as giant urticaria, serum sickness and transfusion reactions) and in acutely increased intracranial pressure.

- **Hydrocortisone: 5 -10 mg/kg/dose ...I.V. or I.M.... every 6 hours.**

Parenteral hydrocortisone is mainly used in acute severe asthma. In asthma, therapy can be continued for 2 - 3 days, after which, the drug can be substituted with one of the oral preparations for another 3 - 4 days.

* Available preparations are:

RI Solu-cortef vial (100 mg/2 ml).
RI Flebocortid amp. (100 mg/2 ml).
RI Hydrocortisone amp. (100 mg/2 ml).

- **Methylprednisolone: 0.5-1.0 mg/kg/dose ... I.V. or I.M. ... every 6 hours.**

It is used in acute severe asthma. The drug is more expensive than hydrocortisone.

* Available preparations are:

Rl Solu-medrol vial (40 mg).
Rl Solu-medrol vial (100 mg).
Rl Solu-medrol vial (500 mg).

- **Dexamethasone: 0.25 - 0.5 mg/kg/dose ... I.V. or I.M., every 12 hours.**

Parenteral dexamethasone is mainly used in acutely increased intracranial pressure, neonatal brain oedema and in severe acute allergic conditions. It can be also used in acute severe asthma when hydrocortisone is not available. In less urgent conditions, the drug can be used by the I.M. route. Therapy is continued for few days, after which, oral preparations can be used when steroid therapy is still needed.

* Available preperations are:

Rl Fortecortin amp. (8 mg/2 ml).
Rl Epidron amp. (8 mg/2 ml).
Rl Dexonium amp. (8 mg/2 ml).
Rl Dexamethazone amp. (8 mg/2 ml).

- **Betamethasone: (Similar to dexamethasone)**

It can be used for the same indications and same dosage of dexamethasone.

* Available preparation is:

Rl Celestone amp. (6 mg/ml).

B) Oral corticosteroids

These drugs are mainly used in chronic conditions or following parenteral therapy in acute life threatening conditions. For **short-term use,** either short-acting drugs (prednisone, prednisolone) or long-acting drugs (dexamethasone, betamethasone) can be used. For **long-term therapy** (over weeks or months), long-acting drugs are contraindicated and short-acting drugs are the only suitable drugs.

- **Hydrocortisone: 2 mg/kg/day ... oral.**

Oral hydrocortisone is mainly used as a replacement therapy in chronic adrenal insufficiency. Treatment is life-long.

* Available preparations are:

Rl Hydrocortone tablets (10 mg).
Rl Hydrocortone tablets (20 mg).

- **Prednisone or prednisolone: 2 mg/kg/day ... oral.**

The daily dose is divided into 3 - 4 doses.

Prednisone is a prodrug (inactive), and it should be converted in the liver to

prednisolone (active). Since there is 20% loss of activity on conversion to prednisolone and since hepatic disease may further impair conversion, prednisolone is preferable than prednisone. Prednisone or prednisolone are mainly used in:

1. Rheumatic diseases: Rheumatic carditis, rheumatoid arthritis and systemic lupus erythematosus.
2. Nephrotic syndrome and other chronic glomerular diseases.
3. Chronic severe asthma.
4. Hematological conditions: Idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, acute leukemia and aplastic anemia.

When chronic therapy is indicated, treatment should be continued with the "alternate-day therapy", after the initial control with the "daily therapy".

* Available preparations are:

* **Prednisone:** ***RI Hostacorten tablets (5 mg).***

* **Prednisolone:** *Syrups:* ***RI Predsol syrup (5 mg/5 ml).***
RI Xilone syrup (5 mg/5 ml).
RI Predsol forte OR Xilone forte syrup (15 mg/5 ml).

Tablets: ***RI Hostacorten-H tablets (5 mg).***
RI Predilon OR Deltacortil tablets (5 mg).
RI Prednisolone tablets (5 mg).

* **Methylprednisolone tablets:** ***RI Urbason tablets (4 mg).***
RI Urbason tablets (8 mg).

• **Dexamethasone or Betamethasone: 0.1 - 0.2 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses.

These drugs are more expensive than prednisone and prednisolone and they are not suitable for long-term use. They are mainly used for short-term therapy in allergic conditions or following parenteral preparations in acute conditions as asthma. The main advantage of these drugs is their availability in syrup forms suitable for young children.

* Available preparations are:

* **Dexamethasone:** *Syrups:* ***RI Phenadone syrup (0.5 mg/5 ml).***
RI Orazone OR Apidone syrup (0.5 mg/5 ml).
RI Vendexine OR Dexaphen syrup (0.5 mg/5 ml).

Tablets: ***RI Orazone tablets (0.5 mg).***
RI Dexazone OR Deltazone tablets (0.5 mg).

* **Betamethasone:** *Tablets:* ***RI Betasone tablets (0.5 mg).***
RI Celestone tablets (0.5 mg).

C) Inhalation corticosteroids

1. Preparations for persistent asthma

- **Beclomethasone: 100 mcg/dose ... inhalation ... 3-4 times daily.**

It is used in persistent asthma. The drug exerts a topical effect on the lungs or the nose without significant systemic absorption. Therapy can be continued for prolonged periods as adrenal suppression is unlikely. The main disadvantage of this drug, as well as other inhalation drugs, is that it is not suitable for children below the age of 6 years where cooperation for inhalation is difficult.

* Available preparations are:

RI Becotide OR Beclosone inhaler (50 mcg/puff).
RI Beclo OR Viarex inhaler (50 mcg/puff).

(Practical dosage is 2 puffs ... inhalation through the mouth .. 3 - 4 times daily).

- **Budesinide: 100 - 200 mcg/dose ... inhalation ... twice daily.**

It is used in persistent asthma. The drug has the advantage of longer duration of action, so it is only used twice daily.

* Available preparations are:

RI Pulmicort Turbuhaler 100 (100 mcg/puff).
RI Pulmicort Turbuhaler 200 (200 mcg/puff).

(Practical dosage is one puff... inhalation through the mouth ... twice daily).

- **Fluticasone: 50 - 100 mcg/dose ... inhalation ... twice daily.**

It is used in persistent asthma. The drug has the advantage of longer duration of action, so it is only used twice daily.

* Available preparations are:

RI Flixotide inhaler 50 (50 mcg/puff).
RI Flixotide inhaler 125 (125 mcg/puff).
RI Flixotide Diskus 50 (50 mcg/inhalation).
RI Flixotide Diskus 100 (100 mcg/inhalation).
RI Flixotide Diskus 250 (250 mcg/inhalation).

(Practical dosage is 1-2 puffs or inhalations... through the mouth ... twice daily).

2. Preparations for allergic rhinitis

- **Beclomethasone:** *RI Beconase spray (50 mcg/metered dose).*
- **Budesinide:** *RI Rhinocort spray (50 mcg/metered dose).*
- **Fluticasone:** *RI Flixonase spray (50 mcg/metered dose).*

(Practical dosage is 1-2 puffs … through the nose ... twice daily).

3

Drugs of CNS

1. Sedatives and Hypnotics.
2. Anticonvulsants and Antiepileptics.
3. Psychotropic Drugs.

1. Sedatives and Hypnotics

Five drugs can be used in pediatric practice to allay anxiety (sedation) or to induce sleep (hypnosis).

Chloral hydrate:	15 - 30 mg/kg/dose ... oral.
Phenobarbital:	1.0 - 2.0 mg/kg/dose ... oral.
Diazepam:	0.1 - 0.2 mg/kg/dose ... oral or I.V.
Midazolam:	0.1 - 0.2 mg/kg/dose ... I.V or I.M.
Ketamine:	0.5 - 1.0 mg/kg/dose ... I.V.
	or 3.0 - 7.0 mg/kg/dose ... I.M.

Sedative is a drug, which relieves anxiety without impairing consciousness while **hypnotic** is a drug, which induces sleep. The difference between sedating and hypnotic effects is a matter of dosage. The hypnotic dose is double the dose for sedation.

Sedation or hypnosis is usually needed in pediatric practice prior to certain diagnostic procedures as catheterization, angiography, endoscopy, ECG, EEG or CT scanning. They are also occasionally needed to sedate or to induce sleep in an irritable infant or child.

- **Chloral hydrate: 15 mg/kg/dose ... oral (for sedation).**
  30 mg/kg/dose ... oral (for hypnosis).

The dose can be repeated as required for maintenance of desired sedative or hypnotic state. Total daily dose should not exceed 50 - 60 mg/kg/day.

Chloral hydrate is a safe drug. When it is available, it should be the drug of choice. The only disadvantage of chloral hydrate is its bitter taste so it is better to be added to a juice.

* Available preparation is:

RI Chloral syrup (500 mg/5 ml).

- **Phenobarbital: 1 mg/kg/dose ... oral (for sedation).**
  2 mg/kg/dose ... oral (for hypnosis).

The dose can be repeated as required. Total daily dose should not exceed 5 mg/kg/day. Adverse reactions are uncommon with small doses but with a large single dose, drowsiness may persist for 24 hours.

* Available preparations are:

Oral: *RI Sominaletta syrup (15 mg/5 ml).*
RI Sominaletta tablets (15 mg).
RI Sominal tablets (60 mg).

Parenteral: *RI Sominaletta amp. (40 mg/ml).*

* Phenobarbital is also present with acetylsalicylic acid suppositories in a dose of 10 mg as:

RI Vegaskine infantile supp. (150 mg + 10 mg).

(See antipyretic drugs).

- **Diazepam: 0.1 mg/kg/dose ... oral or slow I.V. (for sedation).**
  0.2 mg/kg/dose ... oral or slow I.V. (for hypnosis).

The dose may be repeated after 30 minutes (if necessary)
Diazepam is mainly used when an immediate effect is needed.

* Available preparations are:

RI Valium OR Valpam amp. (10 mg/2 ml).
RI Neuril OR Farcozepam OR Epival amp. (10 mg/2 ml).
RI Valium OR Valpam syrup (2 mg/5 ml).
RI Valpam OR Neuril OR Farcozepam tablets (2 mg).
RI Valpam OR Neuril OR Farcozepam OR Valinil tablets (5 mg).

* It is also available as rectal tubes to be used at home in emergency situations of febrile convulsions (Not available in Egypt).

RI Diazepam OR Stesolid rectal tubes (5 mg).
RI Diazepam OR Stesolid rectal tubes (10 mg).

- **Midazolam: 0.1 - 0.2 mg/kg/dose ... I.V. or I.M. (for sedation).**

The dose may be repeated after 30 minutes (if necessary).
Midazolam is 3-5 times more potent than diazepam. It has the advantage of sedation without impairment of consciousness.

* Available preparations are:

RI Dormicum amp. (5 mg/ ml).
RI Medathetic amp. (5 mg/ ml).

- **Ketamine: 0.5 - 1.0 mg/kg/dose ... I.V. or**
  3.0 - 7.0 mg/kg/dose ... I.M.

Ketamine is an anesthetic agent used in induction of general anesthesia or in short-term sedation before minor surgery.

* Available preparations are:

RI Ketalar amp. (500 mg/10 ml).
RI Ketamar vial (500 mg/10 ml).

2. Anticonvulsants and Antiepileptics

Anticonvulsants (I.V. drugs)	
First line drugs	
Diazepam:	0.3 - 0.5 mg/kg/dose.
Phenobarbital:	15 - 20 mg/kg/dose.
Phenytoin:	15- 20 mg/kg/dose.
Midazolam:	0.1 - 0.2 mg/kg/hour ... continuous infusion.
Alternative drugs (for refractory cases)	
Paraldehyde:	100 - 200 mg/kg/dose.
Lidocaine:	1 - 2 mg/kg/dose.
Pentobarbital:	2 - 4 mg/kg/dose.
Antiepileptic drugs (Oral drugs)	
Phenobarbital:	3 - 8 mg/kg/day.
Phenytoin:	3 - 8 mg/kg/day.
Carbamazepine:	10 - 20 mg/kg/day.
Sodium valproate:	20 - 30 mg/kg/day.
Clonazepam:	0.1 - 0.2 mg/kg/day.
Ethosuximide:	20 - 30 mg/kg/day.

A) Anticonvulsants

Anticonvulsants are I.V. drugs that used to control the ongoing convulsive fit.

- **Diazepam: 0.3 - 0.5 mg/kg ... I.V. ... over 3 minutes.**

(The drug should not be diluted or mixed with other drugs).

Diazepam is a highly effective drug. It usually brings convulsions under control within few minutes. When necessary, the dose can be repeated after 5 minutes. If an I.V. line cannot be established, the undiluted calculated dose can be given ***rectally*** by a syringe and flexible tube or diazepam rectal tubes can be used. As the drug has a short duration of action (15 - 20 minutes), convulsions may recur unless a long-acting anticonvulsant (as phenobarbital or phenytoin) is given simultaneously. In refractory cases, diazepam can be given by ***constant infusion*** in a dose of 0.2 mg/kg/hour. Practically, 2 ml diazepam (10 mg) are added to 100 ml saline or Ringer's lactate (1mg/10 ml) and continuous infusion is made at a rate of 2 ml/kg/hour. The rate can be changed according to response.

Diazepam is generally a safe drug. However, respiratory arrest may occasionally occur especially with rapid injection or high dosage. If convulsions are not controlled within 5 -10 minutes following injection, one should proceed to other drugs. Available preparations are:

RI Valium OR Neuril OR Valpam OR Farcozepam amp. (10 mg/2 ml).
RI Diazepam OR Stesolid rectal tubes (5 mg) and (10 mg).

- **Phenobarbital: 15 - 20 mg/kg ... over 3 minutes.**

Phenobarbital is the drug of choice in neonatal convulsions. In infancy and children, it should be tried when diazepam fails to control the condition.

After initial control of convulsions, a maintenance therapy (5mg/kg/day, I.V., in 2 divided doses) is indicated when the risk of recurrence is there.

If phenobarbital fails to control the convulsions within 10 minutes following injection, one should proceed to other drugs. However, the dose can be repeated if phenytoin is not available. As the drug can cause respiratory depression, close monitoring of respiration is essential.

* Available preparations are:

RI Sominaletta amp. (40 mg/ml).

- **Phenytoin: 15 - 20 mg/kg ... I.V. ... over 5 minutes.**

(Monitoring of the heart is essential as serious heart block may occur)

Phenytoin is indicated when diazepam and phenobarbital fail to control the ongoing convulsive fit. After initial control of convulsions, a maintenance therapy (5 mg/kg/day, I.V. in 2 divided doses) may be used.

* Available preparations are:

RI Epanutin OR Phenytoin amp. (250 mg/5 ml).
RI Phenytin amp. (100 mg/2 ml).

- **Midazolam: 0.05 - 0.1 mg/kg ... I.V ... over 3 minutes. Then,**
0.1 - 0.2 mg/kg/hour ... continuous infusion.

It is used after failure of the above 3 drugs. Practically, 1 ml midazolam (5 mg) is added to 100 ml saline or Ringer's lactate (1 mg/20 ml) and the infusion is made at a rate of 2 ml/kg/hour

* Available preparations are:

RI Dormicum OR Medathetic amp.(5 mg/ ml).

B) Antiepileptic drugs

Antiepileptics are oral drugs that are given for prolonged periods *(long-term therapy)* to prevent recurrence of convulsions by suppressing the epileptogenic foci.

- **Phenobarbital: 3 - 8 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses.

Side effects are mainly hyperactivity or drowsiness. Altered sleep pattern and depression of cognitive function may occur with prolonged use.

* Available preparations are:

RI Sominaletta syrup (15 mg/5 ml).
RI Sominaletta tablets (15 mg).
RI Sominal tablets (60 mg).

- **Phenytoin: 5 - 8 mg/kg/day ... oral.**

  The daily dose is divided into 2 - 3 equal doses.
  The main side effects are gingival hyperplasia and hirsutism.

* Available preparations are:

RI Epanutin OR Phenytin OR Ipanten suspension (30 mg/5 ml).
RI Phenytoin OR Phenytin OR Ipanten capsules (50 mg).
RI Phenytoin OR Phenytin OR Ipanten capsules (100 mg).

- **Carbamazepine: 10 - 20 mg/kg/day ... oral.**

  The daily dose is divided into 2 - 3 equal doses.
  The main side effects are drowsiness and liver dysfunction.

* Available preparations are:

RI Tegretol suspension (100 mg/5 ml).
RI Tegretol OR Tegral OR Neurotop OR Carbatol tablets (200 mg).
RI Tegretol CR tablets (200 mg).
RI Neurotop retard tablets (300 mg).

- **Sodium valproate: 20 - 30 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 equal doses. In severe cases, the dose can be increased to 40 - 60 mg/kg/day. Side effects are drowsiness and gastric upset.

* Available preparations are:

RI Depakine OR Valpokine OR Valponex syrup (200 mg/ml).
RI Depakine OR Epilim tablets (200 mg).
RI Convulex drops (300 mg/ml = 10 mg/drop).
RI Convulex capsules (150 mg) and (300 mg).

With Depakine syrup, a graduated pipette (in mg) is included with the bottle for proper calculation of dosage. With Convulex drops, the practical dosage is one drop/kg/dose, every 12 hours.

- **Clonazepam: 0.1 - 0.2 mg/kg/day ... oral.**

  The daily dose is divided into 2 - 3 doses. The main side effect is drowsiness.

* Available preparations are:

RI Rivotril OR Apetryl OR Amotryl OR Klozepam tablets (0.5 mg).
RI Rivotril OR Apetryl OR Amotryl OR Klozepam tablets (2 mg).
RI Rivotril drops (0.1 mg/drop).

(Practical dosage: one drop/kg/day ... divided into 2 - 3 doses).

- **Ethosuximide: 20 - 30 mg/kg/day ... oral.**

  The daily dose is divided into 2 doses. The main side effect is drowsiness.

* Available preparations are:

RI Zarontin syrup (250 mg/5 ml).
RI Zarontin tablets (250 mg).

Recent Antiepileptic Drugs

Lamotrigine:	5 - 15 mg/kg/day ... oral.
Gabapentin:	20 - 50 mg/kg/day ... oral.
Topiramate:	1 - 10 mg/kg/day ... oral.
Vigabatrin:	30 -100 mg/kg/day ... oral.

- **Lamotrigine: 5 -15 mg/kg/day ... oral.**

The daily dose is divided into 2 doses (every 12 hours).

Treatment starts with low dosage (2 mg/kg/day) for 2 weeks then the dose is increased to 5 mg/kg/day for another 2 weeks. Maintenance dose is 5-15 mg/kg/day, divided into 2 doses. If the drug is added to valproate, the dose should be only 1-5 mg/kg/day.

The drug stabilizes neural membrane and inhibits neuronal release especially glutamate. It can be used as a monotherapy in absence seizures or used in addition to other antiepileptic drugs for generalized tonic-clonic seizures.

Side effects may include Stevens-Johnson syndrome and angioedema.

* Available preparations are:

RI Lamictal tablets (25 mg), (50 mg) and (100 mg).
RI Lamotrine tablets (25 mg) and (100 mg).

- **Gabapentin: 20 - 50 mg/kg/day ... oral (divided into 3 doses).**

The drug binds to glutamate synapses and increases brain GABA turnover. It can be also used in addition to other antiepileptic drugs for refractory complex partial seizures or partial seizures with generalized tonic-clonic seizures.

Side effects include somnolence, dizziness, ataxia, nystagmus and tremors.

* Available preparations are:

RI Gaptin OR Conventin capsules (100 mg).
RI Gaptin OR Conventin OR Neurontin capsules (400 mg).

- **Topiramate: 1 - 10 mg/kg/day ... oral (divided into 2 doses).**

The drug blocks the voltage-dependent Na channels. It can be also used in addition to other antiepileptic drugs for refractory complex partial seizures or partial seizures with generalized tonic-clonic seizures.

* Available preparations are:

RI Topamax OR Topiramate tablets (25 mg) and (100 mg).

- **Vigabatrin: 30 - 100 mg/kg/day ... oral (divided into 2 doses).**

The drug increases GABA level. It is useful in infantile spasms, particularly in children with tuberous sclerosis.

* Available preparation is:

RI Sabril tablets (500 mg).

3. Psychotropic Drugs

Psychotropic drugs are drugs that affect the behavior.

Psychostimulants

Methylphenidate:	10 - 40 mg/kg/day ... oral.
Dextroamphetamine:	5 - 20 mg/kg/day ... oral.

Antidepressants

Tricyclics

Imipramine:	2 - 3 mg/kg/day ... oral.
Clomipramine:	2 - 3 mg/kg/day ... oral.
Amitryptyline:	2 - 3 mg/kg/day ... oral.

Selective serotonin reuptake inhibitors (SSRIs)

Fluoxetine:	10-20 mg/day ... oral.
Paroxetine:	10-20 mg/day ... oral.
Sertraline:	25-50 mg/day ... oral.

Antipsychotics

Traditional or typical drugs

Chlorpromazine:	2 mg/kg/day ... oral. (Low-potency/high-dosage)
Haloperidol:	0.1- 0.2 mg/kg/day ... oral. (High- potency/low- dosage)

Atypical new drugs

Resperidone:	2 - 4 mg/day ... oral (in divided doses).
Olanzapine:	5 -15 mg/day ... oral (in divided doses).
Clozapine:	25-50 mg/day ... oral (in divided doses).
Ziprasidone:	40-80 mg/day ... oral (in divided doses).

The use of psychotropic drugs in children should be only carried out by child psychiatrist or highly experienced pediatrician. Therapeutic effect of these drugs usually takes about 2 weeks to appear. Discontinuation of the drug, should be made by a "slowly tapering regimen" to minimize withdrawal symptoms.

A) Psychostimulants

These drugs are mainly used in school-age children with attention deficit hyperactivity disorder (ADHD).

- **Methylphenidate: 10 - 40 mg/day ... oral.**

Start therapy with 10 mg/day. The daily dose is divided into 2 doses, 5 mg (1/2 tablet) at 8 a.m. and another 5 mg (1/2 tablet) at 12.00 Noon. The dose can be gradually increased at weekly intervals by increments of 5 mg/dose, according to the response. Total daily dose should not exceed 1.0 mg/kg/day. To avoid insomnia, the drug should not be used in the afternoon. It is wise to discontinue the drug periodically (every summer) to see if the symptoms are abating or not. Some rebound phenomena may occur for few days or weeks.

RI Ritalin tablets (10 mg).

- **Dextroamphetamine: 5 - 20 mg/day ... oral.**

It is used with the same schedule of methylphenidate. Start therapy with 5 mg/day. The daily dose is divided into 2 doses, 2.5 mg (1/2 tablet) at 8 a.m. and another 2.5 mg (1/2 tablet) at 12.00 Noon. The dose can be gradually increased at weekly intervals by increments of 2.5 mg/dose, according to the response. Total daily dose should not exceed 0.5 mg/kg/day.
* Available preparation is:

RI Dexedrine tablets (5 mg).

B) Antidepressants

1. Tricyclic antidepressants are mainly used in *major depression.* Other indications are *nocturnal enuresis* (impramine) and *obsessive-compulsive disorder* (clomipramine). As antidepressant, the dose is **2-3 mg/kg/day.** For enuresis, the dose is **25 - 50 mg/day ... oral ... once at night** (see enuresis).

Overdosage above 3.5-5 mg/kg/day is serious and may lead to hypertension, cardiac arrhythmias and death. The triad of coma, convulsions and cardiac disturbances is the classic presentation of imipramine poisoning, so the drug should be kept out of reach of the child to avoid accidental poisoning.
* Available preparations are:

- **Imipramine:** *RI Tofranil tablets (10 mg).*
  RI Tofranil tablets (25 mg).
- **Clomipramine:** *RI Anafranil tablets (10 mg).*
  RI Anafranil tablets (25 mg).
- **Amitriptyline:** *RI Tryptizol tablets (10 mg).*
  RI Tryptizol tablets (25 mg).

2. Selective serotonin reuptake inhibitors (SSRIs) are used in *mild to moderate depression, anxiety* and *obsessive-compulsive disorder.* The dose is **10-20 mg/kg/day** (fluoxetine, paroxetine) or **25-50 mg/kg/day** (sertraline).

Side effects include gastrointestinal manifestations (anorexia, nausea, vomiting) and CNS effects (agitation, insomnia, headache, jitteriness).
* Available preparations are:

- **Fluoxetine:** *RI Philozac OR Fluozac capsules (10 mg).*
  RI Philozac OR Prozac OR Florosin capsules (20 mg).
- **Paroxetine:** *RI Seroxat OR Paxetin OR Xandol tablets (20 mg).*
- **Sertraline:** *RI Lustral OR Seserine tablets (50 mg).*
  RI Moodapex OR Sirto tablets (50 mg).

C) Antipsychotics

1. Typical (traditional) antipsychotics are used in psychotic states and severe behavioural disorders. They induce a state of calm without causing sleep. The main indications in pediatric practice are: (1) Severe anxiety and agitation. (2) Aggressive behaviour especially in mentally retarded patients. (3) Childhood and adolescent schizophrenia. (4) Stereotypic movements (haloperidol is the drug of choice in rheumatic chorea). The main side effects, in therapeutic dosage, are sedation and anticholinergic effects (dry mouth, constipation and blurred vision).

- **Chlorpromazine: 2 mg/kg/day ... oral (in 2-3 divided doses).**

The daily dose is divided into 2-3 doses. It induces quietening, indifference and psychomotor slowing. It is very useful to "tame" hyperactive and aggressive behaviour. Available preparations are:

RI Neurazine OR Largactil OR Bromacid tablets (25 mg).

- **Haloperidol: 0.1 - 0.2 mg/kg/day ... oral (in 2 divided doses).**

The daily dose is divided into 2 equal doses. It is also useful in intractable tics and rheumatic chorea. Available preparations are:

RI Safinace tablets (1.5 mg) and (5 mg).

2. Atypical (new) antipsychotics are used in childhood and adolescent schizophrenia and they largely replaced the typical drugs. They have the main side effects of typical drugs but to a lesser extent.

- **Resperidone: 2 - 4 mg/day ... oral (in 2 divided doses).**

Start with 0.5 mg twice daily and increase gradually to 2-4 mg/day.

RI Risperdal OR Psychodal OR Apexidone tablets (1 mg).

RI Risperdal OR Zesperone OR Risdal tablets (2 mg).

- **Olanzapine: 5 -15 mg/day ... oral (in 2 divided doses).**

Start with 2.5 mg twice daily and increase gradually to 10-15 mg/day.

RI Zyprexa tablets (5 mg) and (10 mg).

- **Clozapine: 25-50 mg/day ... oral (in 2 divided doses).**

Start with 6.5 mg twice daily and increase gradually to 25-50 mg/day.

RI Clozapex OR Leponex tablets (25 mg).

- **Ziprasidone: 40-80 mg/day ... oral (in 2 divided doses).**

Start with 6.5 mg twice daily and increase gradually to 25-50 mg/day.

RI Zeldox capsules (40 mg) and (80 mg).

4

Cardiovascular Drugs

1. Inotropic Drugs.
2. Antiarrhythmic Drugs.
3. Antihypertensives.
4. Diuretics.

1. Inotropic Drugs

Inotropic drugs are drugs that increase myocardial contractility and improve cardiac output.

Cardiac glycosides

Digoxin (rapid action): 0.05 mg/kg ... I.V., I.M. or oral (digitalizing dose).
0.01 mg/kg/day I.V., I.M. or oral (maintenance).

Digitoxin (slow action): Same dosage as digoxin. Rarely used.

Sympathomimetic catecholamines

Adrenaline (α, β_1 and β_2 effects): 0.1 -1.0 mcg/kg/minute ... I.V. infusion.
Isoproterenol (β_1 and β_2 effect): 0.1 - 1.0 mcg/kg/minute ... I.V. Infusion.
Dopamine (β_1 and dopaminergic effect): 2 - 20 mcg/kg/minute ... I.V. infusion.
Dobutamine (mainly β_1 effect): 2 - 20 mcg/kg/minute ... I.V. infusion.

Notice

- **Alpha effect:** Peripheral vasoconstriction and hypertension.
- **Beta 1 effect:** Inotropic effect (increase myocardial contractility).
- **Beta 2 effect:** Bronchial dilatation and may be tremors.
- **Dopaminergic effect:** Increased renal blood flow.

	Cardiac glycosides	Sympathomimetic catecholamines
Indications	Acute or chronic congestive heart failure.	ONLY in severe acute congestive heart failure.
Route	I.V., I.M. or oral.	Continuous I.V. infusion.
Half-life	Very long (few days).	Very short (few minutes).
Dosage	In mg/kg/day. (Loading and maintenance)	In microgm/kg/minute. (Immediate effect)
Effect on heart rate	Negative chronotropic effect. (SLOW heart rate)	Positive chronotropic effect. (RAPID heart rate)
Extracardiac Effects	Minimal.	Significant.

A) Cardiac glycosides

1. Cardiac glycosides are the mainstay in management of acute and chronic congestive heart failure:
   * Digoxin is suitable for acute failure (I.V.)
   * Digoxin or digitoxin is suitable for chronic failure (oral). Digoxin is suitable for all purposes and should be the drug of choice.
2. These drugs produce their inotropic effect through increasing the local myocardial catecholamines and increasing intracellular calcium.
3. The half-life of these drugs is long (few days), so their effect continues for days after discontinuation of therapy.
4. They can be given I.V., I.M. or orally.
5. Dosage is calculated as mg/kg/day in a loading (digitalizing) and maintenance doses. The therapeutic range of dosage is narrow, i.e. the difference between therapeutic and toxic doses is small.
6. They have a negative chronotropic effect. i.e. they induce slowing of the heart rate.
7. At therapeutic dosage, the extracardiac effects are minimal.
8. As the therapeutic effect is essentially the same, only ONE drug is used (with catecholamines, more than one drug can be used simultaneously e.g. dopamine and dobutamine).

- **Digoxin: 0.05 mg/kg ... I.V., I.M. or oral, divided (digitalization).**
  0.01 mg/kg/day ... I.V., I.M. or oral (maintenance).

The digitalizing dose is divided into 3 doses as follow:
- 1/2 dose ... initially.
- 1/4 dose ... after 8 hours.
- 1/4 after another 8 hours.

The maintenance dose is divided into 2 equal doses (every 12 hours).

* *Parenteral digoxin therapy* is indicated in acute severe congestive failure. As the patient can tolerate oral feeding, maintenance dose is given orally.

* *Oral digoxin therapy* is indicated in mild to moderate acute failure and in chronic congestive failure. When slow digitalization is required, as in mild chronic congestive failure, the maintenance dose can be given without digitalization. With this regimen, full digitalization can be achieved in 7-10 days.

Important signs of toxicity are vomiting and cardiac arrhythmias.

* Available preparations are:

RI Lanoxin Digoxin amp. (0.5 mg/2 ml).
RI Lanoxin Digoxin tablets (0.25 mg).
RI Cardixin tablets (0.25 mg).
RI Lanoxin Digoxin pediatric elixir (0.05 mg/ml).

- **Practical digitalizing dose is:** - 1.0 ml/5 kg (I.V. or I.M.).
  - 1.0 tablet/5 kg (oral for children).
  - 1.0 ml/kg of pediatric elixir (oral).

Examples

- **1 year old infant (10 kg) with acute severe congestive heart failure.**

  RI Lanoxin Digoxin amp. (0.5 mg/2 ml).

  Give: 1.0 ml I.V. ... then 1/2 ml after 8 hours and 1/2 ml after another 8 hours. Then: 0.2 ml I.V. ... every 12 hours.

- **6 years old child (20 kg) with acute moderate congestive HF.**

  RI Lanoxin Digoxin OR Cardixin tablets (0.25 mg).

  Give: 2 tablets initially ... then one tablet after 8 hours and one tablet after another 8 hours. Then: 1/2 tablet every 12 hours.

- **3 months old infant (5 kg) with chronic mild congestive HF.**

  RI Lanoxin Digoxin pediatric elixir (0.05 mg/ ml).

  Give: 1/2 ml every 12 hours (maintenance without digitalization).

Precautions during digitalis therapy

1. Dose adjustment: The digitalizing and maintenance doses can be slightly increased or decreased according to the response. In the newborn and in late childhood, it is better to lower the digitalizing dose to 0.04 mg/kg. The dose should be also reduced in case of hypoxemia, myocarditis or renal disease.

2. Measurement of serum digoxin level: Mainly in 2 conditions:
- When standard dosage is associated with unsatisfactory therapeutic response.
- When digitalis toxicity is clinically suspected.

Therapeutic digoxin level is 2-4 ng/ml (in infants) and 1-2 ng/ml (in children).

3. Concomitant drug therapy: Drugs as calcium or atropine should be avoided. When diuretics are concomitantly used, hypokalemia should be avoided, as it will predispose to digitalis toxicity.

4. Treatment of toxicity: Early recognition of digitalis toxicity is very important, not only for immediate discontinuation of the drug but also for appropriate treatment of any serious arrhythmias.

1. Continuous ECG monitoring is very important.
2. Atropine (0.01 mg/kg/dose ... I.V.) is effective in digoxin induced sinus bradycardia or A-V block of the second or third degree. The dose may be repeated within few minutes, when necessary.
3. Phenytoin (3-5 mg/kg/dose,I.V., over 5 minutes) is effective in digoxin induced ventricular arrhythmias. The dose may be repeated every 10 minutes, when necessary, up to a total dose of 20 mg/kg.
4. Serum electrolytes should be checked and abnormalities should be corrected especially hypokalemia.

B) Sympathomimetic catecholamines

1. Sympathomimetic catecholamines are used in cardiogenic shock.

- **Adrenaline** is mainly used in cardiopulmonary resuscitation.
- **Isoproterenol** is mainly used when severe bradycardia is also present.
- **Dopamine** is used in cardiogenic shock especially when associated with severe hypotension and vasoconstriction.
- **Dobutamine** can be used instead of dopamine or both drugs can be used together.

2. These drugs produce their inotropic effect through stimulation of beta 1 (cardiac) adrenergic receptors.
3. The half-life of these drugs is very short (few minutes), so, their effect disappears within few minutes of stopping treatment.
4. They are only given by continuous I.V. infusion.
5. Dosage is calculated as microgram/kg/minute. The therapeutic range of dosage is wide. The dose may be increased up to 10 times the initial dose (dose dependent effect).
6. They have a positive chronotropic effect ... i.e., they increase the heart rate. This effect is more prominent with isoproterenol and adrenaline.
7. At therapeutic dosage, extracardiac effects are significant and differ according to the used drug (see below).
8. More than one drug can be used simultaneously. The commonest combination is dopamine and dobutamine.

	Adrenaline	Isoproterenol	Dopamine	Dobutamine
Effects	Alpha Beta 1 Beta 2	Beta 1 Beta 2	Beta 1 Dopaminergic and alpha (at high dose)	Beta 1
Inotropic Effect	+++	+++	++	++
Heart rate	++	+++	0/++	0/+
B.P.	+	—	+	—
Bronchial Dilatation	++	++++	+	+
Vasoconstriction	+++	—	0/+	—
Renal Blood flow	—	—	+	—

- **Adrenaline: 0.01 mg/kg/dose ... I.V. (resuscitation).**
  0.1 - 1.0 mcg/kg/minute (continuous I.V. infusion).

Adrenaline (epinephrine) has an alpha effect (vasoconstriction), beta-1 effect (inotropic action) and beta-2 effect (Bronchial dilatation).

The inotropic effect is strong, so, it is the main catecholamine used in cardiopulmonary resuscitation. It also produces marked tachycardia. (See also bronchodilators and antihistamines).

* Available preparation is:

RI Adrenaline amp. (1.0 mg/ml).

- **Isoproterenol: 0.1 - 1.0 mcg/kg/minute (continuous I.V. infusion).**

(Start with low dosage and increase gradually according to the response).

Isoproterenol has a beta-1 (inotropic) and beta-2 effects (bronchial dilatation). The inotropic effect is almost as that of adrenaline, but the effect on bronchi (bronchial dilatation) and on heart rate (tachycardia) are more than that of adrenaline, so it is mainly used in:

1. Acute severe congestive heart failure (with bradycardia).
2. Severe A-V block not responding to atropine.

* Available preparation is:

RI Isuprel OR Isoprenol amp. (0.2 mg/ ml).

- **Dopamine: 2.0 - 20 mcg/kg/minute (continuous I.V. infusion).**

Dopamine has a beta-1 effect (inotropic action) and dopaminergic effect (increased renal blood flow). At high dosage (above 10 mcg/kg/minute), it has an alpha effect (peripheral vasoconstriction).

Dopamine is mainly used in acute congestive heart failure with cardiogenic shock. The main advantage of the drug over other drugs is its dopaminergic effect on renal blood flow.

Treatment is started with low dosage (2-5 mcg/kg/minute), which can be increased gradually (every few hours) till the desired effect is obtained. In exceptional refractory cases, dosage may reach up to 40 mcg/kg/minute. Withdrawal of the drug should be also gradual.

Both dopamine and dobutamine can be used simultaneously.

* Available preparation is:

RI Intropin OR Dopamine amp. (200 mg/5 ml).

- **Dobutamine: 2.0 - 20 mcg/kg/minute (continuous I.V. infusion).**

Dobutamine has mainly a beta-1 effect (inotropic effect). The main advantage of the drug over other catecholamines is its minimal effect on heart rate, so it is the preferable drug in patients with marked tachycardia. Dobutamine can be used simultaneously with dopamine as an effective substitute to high dose dopamine therapy (above 10 mcg/kg/minute).

It is mainly used in cardiogenic shock and septic shock.

* Available preparation is:

RI Dobutrex OR Dobutamine vial (250 mg).

(To reconstitute, add 10 ml glucose 5% or sterile water to the contents of the vial. The reconstituted solution has the concentration of 25 mg/ml. Saline should not be used for reconstitution).

Dilution and infusion rate of catecholamines

The main practical problem in usage of catecholamines is how to prepare the diluted solution and how to calculate the rate of infusion... i.e. how to translate the dosage in mcg/kg/minute into ml/hour.

1. Dilution: Catecholamines should be diluted as follow:

- ***Adrenaline:*** Add one ampoule (1 mg) to 100 ml glucose 5%. In this solution, each 1 ml contains 10 mcg, i.e. concentration is (10 mcg/ml).
- ***Isoproterenol:*** Add 5 ampoules (1 mg) to 100 ml glucose 5%. In this solution, the concentration is (10 mcg/ml).
- ***Dopamine:*** Add 100 mg to 100 ml glucose 5% (or one ampoule 200 mg to 200 ml glucose 5%). The concentration is (1000 mcg/ml).
- ***Dobutamine:*** Add 100 mg to 100 ml glucose 5% (or the contents of reconstituted vial 250 mg to 250 ml glucose 5%). The concentration is (1000 mcg/ml).

So: Concentration with adrenaline or isoproterenol is (10 mcg/ml) and concentration with dopamine or dobutamine is (1000 mcg/ml).

2. Infusion rate: The rate of infusion in ml/hour is calculated from the following formula:

$$\text{Infusion rate (ml/hour)} = \frac{\text{Weight (kg) x Dose (mcg/kg/min) x 60 (min/h.)}}{\text{Concentration (mcg/ml)}}$$

Practical examples

- **Give isoproterenol infusion to a child (20 kg) in a dose of 0.1 mcg/kg/minute.**
  - Dilution: 5 ampoules (1 mg) to 100 ml glucose 5% (10 mcg/ml).
  - Infusion rate (ml/hour) = $\frac{20 \times 0.1 \times 60}{10}$ = 12 ml/hour.
- **Give dopamine infusion to a child (10 kg) in a dose of 5 mcg/kg/minute.**
  - Dilution: one ampoule (200 mg) to 200 ml glucose 5% (1000 mcg/ml).
  - Infusion rate (ml/hour) = $\frac{10 \times 5 \times 60}{1000}$ = 3 ml/hour.

- **Give dobutamine to a child (15 kg) in a dose of 7 mcg/kg/minute.**

  - Dilution: one vial (250 mg) to 250 ml glucose 5% (1000 mcg/ml).

  - Infusion rate = $\frac{15 \times 7 \times 60}{1000}$ = 5.4 ml/hour.

Simple alternative method of dilution and infusion rate

In this method, the dilution depends on the weight of the patient:

- **For adrenaline or isoproterenol:** Add (0.6 mg x body weight) to 100 ml glucose 5%. In this solution:
Each 1 ml/hour equals to 0.1 mcg/kg/minute. So: 0.3 mcg/kg/minute = 3 ml/hour. and 0.7 mcg/kg/minute = 7 ml/hour, and so on.

- **For dopamine or dobutamine:** Add (6 mg x body weight) to 100 ml glucose 5%. In this solution:
Each 1 ml/hour equals to 1.0 mcg/kg/minute. So: 4 mcg/kg/minute = 4 ml/hour. and 8 mcg/kg/minute = 8 ml/hour, and so on.

Practical examples

- **Give adrenaline to a child (10 kg) in a dose of 0.1 mcg/kg/minute.**
  - Dilution: add (0.6 x 10 = 6 mg = 6 ampoules) to 100 ml glucose 5%.
  - Infusion rate: 0.1 mcg/kg/minute = 1 ml /hour.

- **Give dopamine to a child (15 kg) in a dose of 5 mcg/kg/minute.**
  - Dilution: add (6 x 15 = 90 mg = 2.25 ml) to 100 ml glucose 5%.
  - Infusion rate: 5 mcg/kg/minute = 5 ml /hour.

2. Antiarrhythmic Drugs

Drugs for bradyarrhythmias

Atropine:	0.01 mg/kg/dose ... I.V.
Isoproterenol:	0.1 - 1 .0 mcg/kg/minute continuous I.V. infusion.

Drugs for supraventricular tachyarrhythmias

Adenosine:	0.1 - 0.2 mg/kg/dose ... I.V. bolus.
Verapamil:	0.1 - 0 2 mg/kg/dose ... I.V. over 2 minutes.
Propranolol:	0.1 - 0.2 mg/kg/dose ...slow I.V.
Digoxin:	0.05 mg/kg ... I.V., divided (rapid digitalization in 6-12 hours).

Drugs for ventricular tachyarrhythmias

Lidocaine:	1 mg/kg/dose ... slow I.V.
Phenytoin:	3 - 5 mg/kg/dose ... I.V. over 5 minutes.
Amiodarone:	5 mg/kg/dose ... I.V. over one hour.
Quinidine:	30 mg/kg/day ... oral.

A) Drugs for bradyarrhythmias

Sinus bradycardia and A-V block (heart block) are commonly seen with digitalis toxicity. Treatment is indicated in 2nd and 3rd degree heart block. Severe persistent bradycardia is a sign of decompensation in critically sick patients and is also common during cardiopulmonary resuscitation in patients with unexpected cardiopulmonary arrest.

- **Atropine: 0.01 mg/kg/dose ... I.V.**

(The dose may be repeated every 2 minutes, when necessary, up to 4 doses).

Atropine is an anticholinergic drug that blocks the post-ganglion cholinergic receptors and prevents acetylcholine from exerting its muscarinic action. It increases the heart rate through reducing the vagal tone.

Atropine is also used as a pre-operative medication to decrease salivary and bronchial secretions. It is also used as antidote in organophosphate insecticide poisoning (see comatose child).

* Available preparation is:

RI Atropine sulphate amp. (1 mg/ ml).

(Dilution: one ampoule + 9 ml normal saline. Dose is 0.1 ml/kg ... I.V.).

- **Isoproterenol: 0.1 - 1.0 mcg/kg/minute... continuous I.V infusion.**

It is indicated in severe persistent bradycardia not responding to atropine.

* Available preparation is:

RI Isuprel amp. (0.2 mg/ ml).

(For dilution and infusion rate, see inotropic drugs).

B) Drugs for supraventricular tachyarrhythmias

Paroxysmal atrial tachycardia and atrial flutter are the main indications.

- **Adenosine: 0.1- 0.2 mg/kg/dose ... I.V. bolus.**

The first dose (0.1 mg/kg) can be followed by a second dose after 2 minutes if the first dose is not effective. A third larger dose (0.2 mg/kg) can be used after another 2 minutes if the second dose is also ineffective.

Adenosine is considered the drug of choice for supraventricular tachycardia (SVT) in adults and children because of its efficacy and safety. As the drug is short acting (less than 1 minute), SVT may reappear within a short time.

* Available preparation is:

RI Adenocard amp. (5 mg/2 ml).

- **Verapamil: 0.1 - 0.2 mg/kg/dose ... I.V. over 2 minutes.**

Verapamil is a *calcium channel blocker*, which is used as an emergency treatment of severe symptomatic cases of paroxysmal atrial tachycardia. The injection usually aborts the attack in less than 5 minutes and returns the heart to normal sinus rhythm. Cardiac monitoring during injection is essential as decreased cardiac output and asystole may occur. Other effects include urticaria, bronchospasm and hypotension.

* Available preparations are:

RI Verapamil OR Isoptin amp. (5 mg/2 ml).

Practical dosage is 0.5 ml/kg of the diluted solution (1 ml + 9 ml saline).

- **Propranolol: 0.1 - 0.2 mg/kg/dose ... slow I.V.**

The dose can be repeated every hour as long as the heart rate tolerates it.

Propranolol is a *beta-blocker*, which prolongs AV conduction and converts SVT to normal rhythm. Side effects include bradycardia and hypotension, therefore, monitoring of the heart during injection is necessary. After control of the acute episode, maintenance therapy (0.5 -1.0 mg/kg/dose ... oral... every 6 hours for few months) may be used to prevent further episodes.

* Available preparations are:

RI Inderal amp. (1 mg/ml) and Inderal tablets (10 mg).

- **Digoxin: 0.05 mg/kg ... I.V. divided (rapid digitalization).**

Digoxin is no longer the first-line therapy of SVT because it may transmit atrial beats to ventricles, which could result in ventricular tachycardia or ventricular fibrillation. When it is used, a rapid digitalization over 6 - 12 hours is made. After control of the acute episode, maintenance therapy (0.01 mg/kg/day ... oral ... for few months) may be used to prevent further episodes.

* Available preparations are:

RI Lanoxin Digoxin amp. (0.5 mg/2 ml).
RI Lanoxin Digoxin tablets (0.25 mg).

C) Drugs for ventricular tachyarrhythmias

- **Lidocaine or Lignocaine: 1.0 mg/kg ... slow I.V.**

The dose may be repeated every 5 - 10 minutes until total dose of 5 mg/kg has been administered. Maintenance therapy can be made by continuous infusion of 20 - 50 microgram/kg/minute.

Lidocaine is a local anesthetic drug. It is the drug of choice for all ventricular arrhythmias. It is also effective in digitalis-induced ventricular arrhythmia.

The drug is contraindicated in presence of complete heart block. Adverse effects are mainly on the CNS and include drowsiness, agitation, disorientation, muscle twitching and may be convulsions.

* Available preparations are:

RI Lidocaine OR Xylocaine vial (1 gm/50 ml) i.e. (20 mg/ml).

- **Phenytoin: 3 - 5 mg/kg ... I.V. ... over 5 minutes.**

The dose may be repeated every 10 minutes, when necessary.
(The maximum loading dose is 20 mg/kg).

Phenytoin is an alternative to lidocaine in all ventricular arrhythmias. It is the drug of choice in digitalis-induced supraventricular and ventricular tachy-arrhythmias. Maintenance therapy can be made with oral preparations in a dose of 3 - 5 mg/kg/day, divided into 2 equal doses (every 12 hours).

* Available preparations are:

RI Epanutin OR Phenytoin amp. (250 mg/5 ml).
RI Epanutin OR Phenytoin capsules (100 mg).

- **Amiodarone: 5 mg/kg ... I.V. ... over one hour... then 5-15 mcg/kg/minute ... continuous infusion.**

Amiodarone is used in management of resistant life-threatening ventricular arrhythmias. It is also used in SVT not responding to other drugs. The main side effects are bradycardia and heart block. Fatigue and nightmares may also occur. Maintenance therapy can be made with oral preparations.

* Available preparations are:

RI Cordarone amp. (150 mg/3 ml).
RI Cordarone OR Farcodaron OR Ronecard tablets (200 mg).

- **Quinidine: 30 mg/kg/day ... oral.**

The daily dose is divided into 4 doses (every 6 hours).

Quinidine is used for oral maintenance therapy in ventricular arrhythmias and after the initial control with I.V drugs. It is also used for oral maintenance therapy in atrial flutter, and after the initial control with digoxin.
It is less toxic than procainamide.

* Available preparation is:

RI Quinidine sulphate tablets (200 mg).

3. Antihypertensive Drugs

Direct vasodilators
- Hydralazine: 0.2 - 0.5 mg/kg/dose ... I.V. or I.M. and 1 - 4 mg/kg/day ... oral.
- Sodium nitroprusside: 0.5 - 5.0 mcg/kg/minute ... continuous I.V. infusion.
- Minoxidil: 0.2 - 0.5 mg/kg/day ... oral (maximum dose is 5 -10 mg/day)

Renin-angiotensin system inhibitors
- Captopril: 0.5 - 2.0 mg/kg/day ... oral.
- Enalapril: 0.1 - 0.4 mg/kg/day ... oral.

Calcium channel blockers
- Nifedipine: 0.25 - 0.5 mg/kg/dose ... oral or sublingual ... every 8 hours.
- Amlodipine: 0.1 - 0.6 mg/kg/day ... oral (maximum dose is 5 mg/day)

Sympatholytic agents
- Methyldopa: 5 -10 mg/kg/dose ... I.V. and 10 - 40 mg/kg/day ... oral.
- Clonidine: 3.0 - 5.0 mcg/kg/day ... oral.

Adrenergic blockers
- Prazosin (alpha blocker): 0.1 - 0.4 mg/kg/day ... oral.
- Propranolol (beta blocker): 1.0 - 4.0 mg/kg/day ... oral.
- Atenolol (beta blocker): 1 - 2 mg/kg/day ... oral.

Diuretics
- Furosemide 2 mg/kg/dose I.V or I.M.
  2 mg/kg/day ...oral.

A) Treatment of hypertensive crisis

Acute severe hypertension (hypertensive crisis) is a serious condition, which may lead to hypertensive encephalopathy or hypertensive heart failure. Urgent therapy with rapidly acting drugs is indicated to prevent these complications. The following drugs are effective:

1. Sublingual nifedipine.
2. I.V. furosemide.
3. I.V. methyldopa.
4. I.V hydralazine.
5. I.V. infusion of sodium nitroprusside.

- **Nifedipine: 0.25 - 0.5 mg/kg/dose ... sublingual or oral.**

The contents of the gelatin capsule are placed sublingually for immediate onset of activity. However, gastrointestinal absorption is also rapid, so it is also effective in hypertensive crisis. The dose can be repeated after 30 - 60 minutes when necessary. The main side effects are facial flushing and tachycardia.

* Available preparations are:

RI Epilat OR Adalat OR Nifepin capsules (10 mg).
RI Epilat OR Adalat retard capsules (20 mg).

• **Furosemide: 2 mg/kg/dose ... I.V or I.M.**

The dose can be repeated after 4 - 6 hours, when necessary. Furosemide is a highly effective loop diuretic (See diuretics).

* Available preparations are:

RI Lasix OR Salex OR Lafurex amp. (20 mg/2 ml).
RI Lasix OR Furosemide OR Lafurex amp. (40 mg/4 ml).

• **Methyldopa: 5 - 10 mg/kg/dose ... I.V. only (not I.M.).**

The dose can be repeated every 6 - 8 hours as required for blood pressure control. It is usually effective in 1 - 2 hours.

Methyldopa produces its hypotensive effect through its metabolite, alpha-methylnorepinephrine, which stimulates CNS alpha-adrenergic receptors, resulting in inhibition of central sympathetic outflow. Cardiac output and renal blood flow remain largely unchanged. The major side effect is sedation. Prolonged use may lead to psychic depression.

After the initial control of blood pressure, treatment can be continued orally.

* Available preparations are:

RI Aldomet amp. (250 mg/5 ml).
RI Aldomet OR Kadomet OR Adamat tablets (250 mg).

• **Hydralazine: 0.2 - 0.5 mg/kg/dose ... I.V. (or I.M.).**

The dose can be repeated every 3 - 6 hours as required for blood pressure control. It is usually effective in 30 minutes.

Hydralazine produces its hypotensive effect through direct arteriolar vasodilatation. The drug has the advantage of improving cerebral and renal blood flow.

Side effects may include headache, anorexia, nausea, sweating and flushing.

* Available preparations are:

RI Apresoline amp. (20 mg/ml).

When the above drugs are ineffective, sodium nitroprusside can be used.

• **Sodium Nitroprusside: 0.5 - 5.0 mcg/kg/minute ... continuous I.V. infusion.**

Start with low dosage of 0.5 mcg/kg/minute and increase the dose gradually according to the response. In most cases, dosage of 2 - 3 mcg/kg/minute is quite effective and should not be exceeded.

Sodium nitroprusside is a potent direct-acting hypotensive drug. It produces its effect through direct arteriolar and venous vasodilatation. It is usually effective within 10 minutes. As the half-life is very short, it is only given by the continuous I.V. infusion.

The drug may be also used as an *"afterload reducing agent"* in acute severe congestive heart failure.

It is important to remember that sodium nitroprusside is rapidly inactivated by light (Photochemical degradation), so, the drip bottle and the tubing system should be covered with aluminium paper (included with the vial).

* Available preparation is:

RI Nipride vial (50 mg + 2 ml glucose 5%).

The contents of the vial are dissolved in 2 ml glucose 5% then the amount (50 mg) is added to 500 ml glucose 5%. The concentration in this solution is (100 mcg/ml). Rate of infusion in ml/hour is calculated from the following formula:

$$\text{Rate (ml/hour)} = \frac{\text{Weight (kg)} \times \text{Dose (mcg/kg/minute)} \times 60 \text{ (min/h.)}}{\text{Concentration (mcg/ml)}}$$

Example: A child (20 kg), dose is 0.5 mcg/kg/minute.

$$\text{Rate (ml/hour)} = \frac{20 \times 0.5 \times 60}{100} = 6 \text{ ml/hour.}$$

Points to remember

1. Frequent or even continuous monitoring of blood pressure is essential to avoid severe hypotension.
2. As most of these drugs may produce postural hypotension, blood pressure should be also measured in sitting position.
3. After initial control, maintenance therapy can be made with oral drugs.

B) Treatment of non-emergency hypertension

The basic rule in management of non-emergency hypertension is to start therapy with ONE oral drug. The starting dose should be low then it can be gradually increased, every 2-3 days, until the desired therapeutic response is achieved. Occasionally, when combined therapy is needed, the TWO drugs should belong to different groups i.e. different mechanisms of action.

(a) Direct vasodilators

- **Hydralazine: 1 - 4 mg/kg/day ... oral.**

The daily dose is divided into 3 - 4 doses (every 6 - 8 hours).

The drug has the advantage of increasing renal and cerebral blood flow. It is the drug of choice for treatment of hypertension in infants. If tachycardia develops, combined therapy with propranolol is indicated. It is also used as an *"afterload reducing agent"* in chronic congestive heart failure.

* Available preparation is:

RI Apresoline tablets (25 mg).
RI Slow Apresoline tablets (50 mg).

• Minoxidil: 0.2 - 0.5 mg/kg/day ... oral.

The daily dose is divided into two doses (every 12 hours) or can be given as a single daily dose. Maximum daily dose is 5 - 10 mg/day.

Monoxidil is a direct arterial vasodilator similar to hydralazine. It has the advantage of longer duration of action so it can be used only twice daily. The main side effects are hypertrichosis (excessive hair growth) and fluid retention.

* Available preparations are:

RI Minoxidil OR Loniten tablets (2.5 mg).
RI Minoxidil OR Loniten tablets (5 mg).

(b) Renin-angiotensin system inhibitors

• Captopril: 0.5 - 2.0 mg/kg/day ... oral.

The daily dose is divided into 3 - 4 doses (every 6 - 8 hours).

Captopril is a potent antihypertensive drug, which exerts its effect through competitive inhibition of angiotensin converting enzyme (ACE). The enzyme is responsible for the conversion of angiotensin I to angiotensin II. The drug is especially useful in hypertension of renal origin.

It is also used as an *"afterload reducing agent"* in chronic congestive heart failure. It produces arteriolar vasodilatation.

Side effects are generally uncommon. Rash, pruritis or fever occurs in few patients. Taste impairment, proteinuria and hypotension are rare.

* Available preparations are:

RI Capoten OR Capotril OR Hypopress tablets (25 mg).
RI Capoten OR Capotril OR Farcopril tablets (50 mg).

• Enalapril: 0.1 - 0.4 mg/kg/day ... oral.

Enalapril is a renin-angiotensin system inhibitor similar to captopril and can be used in the same indications. It has the advantage of longer duration of action so it can be used only twice daily (every 12 hours).

* Available preparations are:

RI Enalapril OR Renitec tablets (5 mg).
RI Lotrial OR Ezapril tablets (10 mg).
RI Enalapril OR Renitec tablets (20 mg).

(c) Calcium channel blockers

• Nifedipine: 0.25 - 0.5 mg/kg/dose ... oral ... every 8 hours.

The contents of gelatin capsule may be placed sublingually for immediate onset of activity. However, gastrointestinal absorption is also rapid, so it is also effective in hypertensive crisis. The dose can be repeated after 30 - 60 minutes when necessary. The main side effects are facial flushing and tachycardia.

* Available preparations are:

RI Epilat OR Adalat OR Nifepin capsules (10 mg).
RI Epilat OR Adalat retard capsules (20 mg).

- **Amlodipine: 0.1 - 0.6 mg/kg/day ... oral.**

Amlodipine has a long duration of action so it is given as a single daily dose (The maximum daily dose is 5 mg/day). In addition to its hypotensive effect, it causes coronary dilatation thus increasing myocardial oxygen supply. The main side effect is facial flushing but without reflex tachycardia.
* Available preparations are:

RI Norvasc OR Alkapress OR Myodura OR Amlodipine tablets (5 mg).
RI Norvasc OR Alkapress OR Myodura tablets (10 mg).

(d) Sympatholytic agents

- **Methyldopa: 10 - 40 mg/kg/day ... oral.**

The daily dose is divided into 3 - 4 doses (every 6 - 8 hours). The main side effects are sedation and psychic depression. * Available preparations are:

RI Aldomet OR Kadomet tablets (250 mg).

- **Clonidine: 3 - 5 mcg/kg/day ... oral.**

The daily dose is given as a single dose or 2 divided doses.
The drug acts through its alpha-2 agonist effect in the CNS. Side effects include sedation, constipation and rebound hypertension with sudden withdrawal.
* Available preparation is:

RI Catapress tablets (150 mcg).

(e) Adrenergic blockers

- **Prazosin (Alpha blocker): 0.1 - 0.4 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses. The initial dose should be only 1 mg (one tablet) per day then, the dose can be increased gradually.
* Available preparations are:

RI Minipress tablets (1 mg) and (2 mg).

- **Propranolol (Beta blocker) : 1 - 4 mg/kg/day ... oral.**

The daily dose is divided into 3 - 4 doses, every 6 -8 hours. Practical dosage is 1 mg/mg/dose, every 6 hours. As the main side effect is bradycardia, combined therapy with hydralazine (produces tachycardia) is indicated. The drug is also useful in hypercyanotic attacks of congenital cyanotic heart disease. The main side effects are bronchospasm and bradycardia.
* Available preparations are:

RI Inderal tablets (10 mg) and (40 mg).

- **Atenolol (Beta blocker): 1 - 2 mg/kg/day ... oral.**

Atenolol has a long duration of action so it is given as a single daily dose. Like propranolol, the main side effects are bronchospasm and bradycardia.
* Available preparations are:

RI Tenormin OR Ateno OR Atelol OR Tenotens tablets (50 mg).

4. Diuretics

Loop diuretics	
Furosemide:	1 - 2 mg/kg/dose ... I.V or I.M and 1 - 2 mg/kg/day... oral.
Bumetanide:	0.01 - 0.1 mg/kg/dose ... I.V, I.M or oral.
Thiazides	
Hydrochlorothiazide:	1 - 2 mg/kg/day... oral.
Potassium sparing diuretics	
Spironolactone:	1 - 2 mg/kg/day... oral.
Carbonic anhydrase inhibitor	
Acetazolamide:	10 - 40 mg/kg/day... oral.
Osmotic diuretics	
Mannitol 20%:	5 - 10 ml/kg ... I.V. (over 30 minutes).

Mechanism of action and efficacy

Diuretics are drugs that increase the urine flow mainly through interfering with reabsorption of filtered sodium by renal tubules. The site of action, efficacy and metabolic effects are different in various groups.

- **Loop diuretics** are highly effective drugs. They cause 20% of filtered sodium to be excreted. The site of action is the ascending limb of loop of Henle. They also cause significant potassium loss (hypokalemia).
- **Thiazides** are moderately effective drugs. They cause 10% of filtered sodium to be excreted. The site of action is the cortical diluting segment. They also cause significant potassium loss (hypokalemia).
- **Potassium sparing diuretics** are mildly effective drugs. They cause 5% of filtered sodium to be excreted. The site of action is the distal tubule. As the sodium loss is through the exchange with potassium, so, there is potassium retention (hyperkalemia). These drugs are mainly used with thiazide to potentiate the diuretic effect and to counteract the effect on potassium ion.
- **Carbonic anhydrase inhibitor,** acetazolamide, is a mildly effective drug. It causes loss of 5% of filtered sodium. The site of action is the distal tubule. It also causes potassium loss (hypokalemia).
- **Osmotic diuretic,** mannitol, acts through raising osmolarity of tubular fluid, thus preventing water reabsorption. The site of action is the proximal tubule. Sodium and potassium losses are proportionate to the osmotic load.

Notice: Drugs that increase cardiac output (inotropic drugs) have some diuretic effect through increasing the glomerular filtration rate. Drinking water causes diuresis through inhibition of release of antidiuretic hormone.

A) Loop diuretics

- **Furosemide: 1 - 2 mg/kg/dose ... I.V. or I.M. (acute conditions)**
  1 - 2 mg/kg/day ... oral (chronic conditions)

Furosemide is the most commonly used diuretic in pediatric practice.

The parenteral form (I.V. or I.M.) is mainly used in:

1. Acute severe edematous states (as in nephrotic syndrome).
2. Acute oliguric renal failure to induce diuresis.
3. Acute congestive heart failure (as a preload reducing agent).
4. Acute severe hypertension (when hypotensive drugs are not available).

The dose can be repeated after 4 - 6 hours, when necessary. In severe cases, it can be increased to 4 - 6 mg/kg.

The oral form is used in non-emergency conditions as:

1. Moderate cases of edema, or after the initial control of severe cases.
2. Chronic congestive heart failure, or after the initial control of acute cases.
3. Chronic hypertension.

The daily dose is divided into 2 - 4 doses. However, with chronic use, the daily dose can be given as a single dose or even every other day.

The main side effect is hypokalemia, so potassium supplementation is important with chronic use (see mineral therapy).

* Available preparations are:

RI Lasix OR Salex amp. (20 mg/2 ml).
RI Lafurex OR Furosemide OR Diusex amp. (20 mg/2 ml).
RI Lasix OR Lafurex OR Furosemide OR Diusex amp. (40 mg/4 ml).
RI Lasix OR Salex OR Lafurex OR Furosemide tablets (40 mg).

- **Bumetanide: 0.01 - 0.1 mg/kg/dose ... I.V., I.M. or oral.**

Bumetanide is a loop diuretic, which has the same therapeutic effects and indications of furosemide. With equivalent dosage, it is a 100 times as effective as furosemide. The dose can be repeated every 6-24 hours.

* Available preparations are:

RI Edemex OR Burinex amp. (0.5 mg/2 ml).
RI Edemex OR Burinex tablets (1 mg).

B) Thiazides

Thiazides are moderately effective drugs that can be used in non-emergency situations as in oedematous states and long-term therapy of congestive heart failure and hypertension.

- **Hydrochlorothiazide: 1 - 2 mg/kg/day ... oral.**

  The daily dose is divided into 2 doses (every 12 hours). It is the most commonly used thiazide.

* Available preparations are:

RI Hydretic OR Hdrozide tablets (12.5 mg).

* It is also available in combination with amiloride (sodium channel blocker):

RI Moduretic tablets (50 mg Hydrochlorothiazide +5 mg amiloride).
RI Yostiretic tablets (50 mg Hydrochlorothiazide +5 mg amiloride).
RI Hydikal tablets (50 mg Hydrochlorothiazide +5 mg amiloride).

C) Potassium sparing diuretics

These mildly effective drugs are not used alone, but usually in combination with thiazides to potentiate their effect and to counteract the effect on potassium ion.

- **Spironolactone: 1 - 2 mg/kg/day ... oral.**

  The daily dose is divided into 2 - 3 doses.

* Available preparations are:

RI Aldactone OR Epilactone tablets (25 mg).
RI Spectone OR Potasave tablets (25 mg).

* Spironolactone is available in combination of Furosemide:

RI Lasilactone tabletas (50 mg Spironolactone + 20 mg furosemide).
RI Fructone capsules (50 mg Spironolactone + 20 mg furosemide).

* Spironolactone is also available in combination of hydrochlorothiazide:

RI Aldactazide tablets (25 mg of each).
RI Spirozide tablets (25 mg of each).

D) Carbonic anhydrase inhibitor

- **Acetazolamide: 10 - 40 mg/kg/day ... oral.**

  The daily dose is divided into 3 - 4 doses (every 6 - 8 hours).

  Acetazolamide is only used in 3 conditions:

1. As adjunct in the treatment of convulsive disorders (ketotic effect).
2. As temporary mean for controlling the progression of hydrocephalus in patients who are not fit for surgery. In this case, dosage may be increased up to 80 mg/kg/day.
3. To lower the increased intracranial pressure in case of pseudotumor cerebri.

* Available preparations are:

RI Diamox tablets (250 mg).
RI Sedamex tablets (250 mg).
RI Hi-Diure tablets (250 mg).

E) Osmotic diuretics

- **Mannitol 20 %: 5 - 10 ml/kg ... I.V. ... over 30 minutes.**

The dose is repeated every 6 hours, for 2 - 3 days.

Mannitol is mainly used for rapid reduction of increased intracranial pressure and reduction of cerebral mass in case of brain oedema. The therapeutic effect is not primarily through diuresis but the increased osmolarity of the blood will draw fluids out of tissues (cellular dehydrating effect).

It may be also used to induce diuresis in patients with oliguric renal failure to change it into non-oliguric renal failure.

* Available preparation is:

RI Mannitol 20% (Bottle of 500 ml).

5

Drugs of Respiratory System

1. Nasal Decongestants.
2. Cough Suppressants.
3. Expectorants and Mucolytics.
4. Bronchodilators (asthma relievers).
5. Asthma Protective Drugs (Asthma controllers).

1. Nasal Decongestants

Nose drops	
Xylometazoline:	1 - 2 drops in each nostril ... 2 - 3 times daily.
Oxymetazoline:	1 - 2 drops in each nostril ... 2 - 3 times daily.
Tetrahydrozoline:	1 - 2 drops in each nostril ... 2 - 3 times daily.
Naphazoline:	1 - 2 drops in each nostril ... 2 - 3 times daily.
Phenylephrine	1 - 2 drops in each nostril ... 2 - 3 times daily.
Oral nasal decongestants	
Phenylephrine:	1 mg/kg/day ... oral.
Phenylpropanolamine:	1 mg/kg/day ... oral.
Etilefrine:	1 mg/kg/day ... oral.
Pseudoephedrine:	3 - 4 mg/kg/day ... oral.

A) Nose drops

Nose drops produce their immediate effect through local vasoconstriction of the congested nasal mucosa. They are ONLY indicated in severe conditions in which nasal obstruction interferes with sleep or food intake.

Nose drops are applied while the child is supine and neck is extended. The dose is 1 - 2 drops instilled in each nostril, 10 minutes before feeding, 2 - 3 times daily. Duration of therapy should not exceed 4-5 days otherwise, chemical rhinitis with continuation of symptoms will occur (nose drops induced rhinitis).

In infants and children, nose drops may cause local irritation and may also affect the ciliary action of nasal mucosa.

- **Xylometazoline:** ***RI Otrivin OR Rhinex OR Balkis pediatric nasal drops.***
- **Oxymetazoline:** ***RI Iliadin OR Afrin OR Oxymet pediatric nasal drops.***
- **Tetrahydrozoline:** ***RI Nazine nasal drops.***
- **Naphazoline:** ***RI Rinosin nasal drops..***
- **Phenylephrine:** ***RI Vibrocil gel and Vibrocil spray.***

Saline nose drops ***(Otrivin saline nasal drops)*** may be used in newborns and infants to relieve nasal obstruction.

B) Oral nasal decongestants

The active drug in these preparations is a sympathomimetic amine, which has a stimulant effect on alpha-adrenergic receptors of the vascular smooth muscles. This leads to vasoconstriction of the arterioles of nasal mucosa and respiratory passages as well. These preparations have some advantages over nose drops. They do not cause local irritation and are unlikely to affect the ciliary action. In addition, they cause shrinkage of the congested mucosa of the sinuses.

The major disadvantage of these drugs is that they also produce dryness of bronchial secretions, thus, interfering with expectoration. So, they should not be used when nasopharyngitis is associated with bronchitis. Duration of therapy should not exceed 5 - 7 days; otherwise, chemical rhinitis may also occur.

- **Phenylephrine: 1 mg/kg/day ... oral.**

The daily dose is divided into 3 doses.

* Available preparations are:

RI Sine-up syrup (5 mg/5 ml).
RI Sine-up tablets (10 mg).

- **Phenylpropanolamine: 1 mg/kg/day ... oral.**

The daily dose is divided into 3 - 4 doses.

* Most available preparations contain paracetamol as well:

RI Rhinomol syrup (5 mg + 120 mg paracetamol/5 ml).
RI Noflu syrup (6.25 mg + 120 mg paracetamol/5 ml).
RI Rhinogesic syrup (10 mg + 120 mg paracetamol/5 ml).
RI Noflu OR Flurest OR Flustop tablets (24 mg + 400 mg paracetamol).

- **Etilefrine: 1 mg/kg/day ... oral.**

The daily dose is divided into 2 doses (every 12 hours).

* Available preparations are:

RI Balkis syrup (6.7 mg/5 ml).
RI Balkis capsules (20 mg).

- **Pseudoephedrine: 3- 4 mg/kg/day ... oral.**

The daily dose is divided into 3 doses. It is recently the most recommended nasal decongestant.

* Most available preparations contain paracetamol or ibuprofen as well:

RI Flumol syrup (15 mg + 120 mg paracetamol/5 ml).
RI Congestal syrup (15 mg + 160 mg paracetamol/5 ml).
RI Michaelon syrup (30 mg + 125 mg paracetamol /5 ml).
RI Brufen Flu syrup (15 mg + 100 mg ibuprofen /5 ml).
RI Dolo-D syrup (15 mg + 100 mg ibuprofen /5 ml).
RI Panadol Sinus tablets (30 mg + 500 mg paracetamol).
RI Flupy-X tablets (30 mg + 500 mg paracetamol).
RI Michaelon tablets (60 mg + 400 mg paracetamol).
RI Congestal tablets (60 mg + 650 mg paracetamol).
RI Brufen Flu tablets (30 mg + 200 mg ibuprofen).
RI Rhinofen tablets (30 mg + 200 mg ibuprofen).
RI Farex tablets (30 mg + 200 mg ibuprofen).
RI Brufen Cold tablets (60 mg + 400 mg ibuprofen).
RI Cataphed tablets (60 mg + 500 mg ibuprofen).

2. Cough Suppressants

There are **eight** available centrally acting cough suppressants.

Pholcodin:	0.5 - 1 mg/kg/day... oral or rectal.
Dextromethorphan:	1 - 2 mg/kg/day... oral.
Clobutinol:	1 - 2 mg/kg/day... oral.
Butamirate:	1 - 2 mg/kg/day... oral.
Oxeladine:	1 - 2 mg/kg/day... oral.
Benproperine:	1 - 2 mg/kg/day... oral.
Noscapine	1 - 2 mg/kg/day... oral.
Pipazethate:	1 - 2 mg/kg/day... oral or rectal.

Mechanism of action and indications for use

Cough suppressants are drugs that suppress the dry unproductive cough (useless cough) through suppressing the cough center.

The use of these drugs should be limited to few indications:

1. ***Whooping cough,*** where cough suppression is useful to allay the dry, spasmodic and nonproductive cough and to minimize the incidence of complications. In this case, the cough suppressant may be used for several weeks.

2. ***Interstitial pneumonia,*** where severe spasmodic cough is marked.

3. ***Severe tracheobronchitis,*** especially during the first few days, when the cough is severe, dry and may be spasmodic. In this case, the use of a cough suppressant for 2-3 days especially at night will help to induce a symptomatic relief and calm sleep. Once the cough is productive, these drugs are contraindicated.

- **Pholcodin: 0.5 - 1.0 mg/kg/day ... oral or rectal.**

Pholcodine does not cause constipation, respiratory depression or habituation.

* Available preparations are:

RI Cyrinol syrup (4 mg + 7 mg ephedrine).
RI Eucaphol pediatric supp. (5 mg).
RI Pyraphol pediatric supp. (5 mg + 200 mg paracetamol).

- **Dextromethorphan: 1 - 2 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses. It is contraindicated in asthma as it causes release of histamine. Available preparations are:

RI Codilar syrup (5 mg/5 ml).
RI Tussivan-N syrup (7.5 mg/5 ml).
RI Neo Pulmolar syrup (15 mg/5 ml).
RI Tussilar tablets (15 mg).

- **Clobutinol: 1 - 2 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses. It has the advantage of rapid onset of action.

* Available preparations are:

Rl Silomat drops (60 mg/ml = 2 mg/drop).
Rl Silomat syrup (20 mg/5 ml).
Rl Silomat tablets (40 mg).

- **Butamirate: 1 - 2 mg/kg/day ... oral.**

The daily dose is divided into 3 - 4 doses. It has the advantage of causing bronchodilatation so it can be used in asthmatics.

* Available preparations are:

Rl Sinecod drops (5 mg/ml = 0.25 mg/drop).
Rl Sinecod syrup (7.5 mg/5 ml).
Rl Cough Cut syrup (7.5 mg/5 ml).

- **Oxeladine: 1 - 2 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses.

* Available preparations are:

Rl Paxeladine OR Oxeladine syrup (10 mg/5 ml).
Rl Paxeladine capsules (40 mg).

- **Benproperine: 1 - 2 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses.

* Available preparations are:

Rl Pectipro syrup (15 mg/5 ml).

- **Noscapine: 1 - 2 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses.

* Available preparations are:

Rl Noscapine syrup (15 mg/5 ml).
Rl Tusscapine syrup (15 mg/5 ml).
Rl Coflin tablets (30 mg).

- **Pipazethate: 1 - 2 mg/kg/day ... oral or rectal.** لو الكحة تشتد عليه بالليل

The daily dose is divided into 2 - 3 doses, or given once at night.

It has the advantage of rapid action and the disadvantage of bitter taste; so, it is better to be added to milk or any other liquid.

* Available preparations are:

Rl Selgon drops (40 mg/ml = 2 mg/drop).
(Practical dosage is one drop/kg/day).
Rl Selgon infantile supp. (10 mg).
Rl Selgon tablets (20 mg).

3. Expectorants and Mucolytics

Expectorants		
	Ammonium chloride:	No accurate dosage.
	Guaiphenesin:	No accurate dosage.
Mucolytics		
	Bromhexine:	0.5 – 1.0 mg/kg/day ... oral.
	Ambroxol:	1.0 - 2.0 mg/kg/day ... oral, I.V. or I.M.
	Carbocisteine:	10 - 20 mg/kg/day ... oral.

A) Expectorants

Expectorants are drugs that increase the secretions of respiratory tract, thus, facilitating effective drainage. The mechanism of action is probably through reflex irritation of gastric mucosa.

There is no scientific evidence that these drugs have any pharmacological action. With best results, the therapeutic value to the patient is minimal, if at all. So, when prescribing these drugs, one should not expect an appreciable response.

Most of the available mixtures contain either ammonium chloride or guaiphenesin as an expectorant. An antihistaminic drug is usually present to act as a sedative. However, antihistamines will cause dryness of secretions and oppose the presumed expectorant effect. As the pharmacological action is doubtful, choice between different mixtures is not critical.

There is no accurate dosage, but roughly:

- In late infancy and early childhood: one teaspoon, 3 times daily.
- In late childhood: two teaspoons, 3 times daily.

Duration of therapy is usually 5 - 7 days.

1. Ammonium chloride containing mixtures

RI Avipect syrup.
RI Bronchistal syrup.
RI Coldal syrup OR Neo-Coldal syrup.
RI Koffex syrup OR Koffex for children syrup.
RI Pulmonal-N syrup.
RI Expectyl syrup.
RI Isilin syrup.
RI Sedaline syrup.

2. Guaiphenesin containing mixtures

RI Bronex pediatric drops.
RI Phenergan expectorant syrup.
RI Actifed expectorant syrup.

3. Mixtures containing both expectorant and cough suppressant

Some mixtures contain an expectorant (as guaiphenesin) and a cough suppressant (dextromethorphan or noscapine) as well. Manufacturers claim that this apparent therapeutic incompatibility is to make cough more productive while also controlling it. Again, choice between all mixtures is not critical.

RI Toplexil syrup.
RI Osinex syrup.
RI Pulmocare syrup.
RI Bronchophane syrup.
RI Oplex syrup.
RI Noscaphen syrup.
RI Rectoplexil pediatric suppository.

B) Mucolytics

Mucolytics are drugs that reduce the viscosity of bronchial secretions, i.e., liquefy the viscid secretions by breakdown of acid mucopolysaccharide fibers.

- **Bromhexine: 0.5 - 1.0 mg/kg/day ... oral.**

The daily dose is divided into 3 doses.
Full therapeutic response usually occurs after 2 - 3 days of onset of therapy.
- Available preparations are:

RI Bisolvon OR Solvin drops (2 mg/ml = 0.1 mg/drop).
RI Bisolvon OR Solvin OR Bromhexine OR Mucolyte syrup (4 mg/5 ml).
RI Bisolvon OR Solvin OR Bromhexine OR Mucolyte tablets (8 mg).

- **Ambroxol: 1.0 - 2.0 mg/kg/day ... oral, I.V. or I.M.**

The daily dose is divided into 2 - 3 doses.
Ambroxol increases respiratory tract secretions, enhances pulmonary surfactant production and stimulates ciliary activity, which results in improved mucous flow and transport (mucokinetic effect).
- Available preparations are:

RI Ambroxol OR Mucosolvan drops (7.5 mg/ml = 0.5 mg/drop).
RI Bronchopro OR Mucosin drops (7.5 mg/ml = 0.5 mg/drop).
RI Ambroxol OR Mucosolvan OR Bronchopro syrup (15 mg/5 ml).
RI Mucosin OR Muco OR Mucofar syrup (15 mg/5 ml).
RI Ambroxol OR Mucosolvan OR Mucosin tablets (30 mg).
RI Mucosolvan amp.(15 mg/2 ml).

- **Carbocisteine: 10 - 20 mg/kg/day ... oral.**

The daily dose is divided into 3 doses. Available preparations are:
RI Carbolase OR Rhinathiol syrup (100 mg/5 ml).
RI Mucosol syrup (125 mg/5 ml).
RI Mucosol OR Mucolase OR Ultrasolv OR Solvex syrup (250 mg/5 ml).
RI Carbolase OR Rhinathiol Mucosol OR Solvex capsules (375 mg).

4. Bronchodilators (or Asthma Relievers)

Sympathomimetic beta adrenergic agonists

Nonselective agonists

Adrenaline: 0.01 mg/kg/dose ... subcutaneous.

Selective beta 2 agonists

Salbutamol: 0.1 - 0.2 mg/kg/day ... oral or inhalation.
Terbutaline: 0.1 - 0.2 mg/kg/day ... oral or inhalation.
Fenoterol: 0.1 - 0.2 mg/kg/day ... oral or inhalation.

Anticholinergic drugs

Atropine: 0.02 - 0.05 mg/kg/dose ... nebulization.
Ipratropium: 20 - 40 mcg/metered dose ... inhalation.

Methylxanthine derivatives

Theophylline: 15 - 20 mg/kg/day ... I.V., oral or rectal.

Corticosteroids

Parenteral and oral forms (see anti-inflammatory drugs).

Adrenergic receptors are 3 types; alpha, beta 1 and beta 2:

- Stimulation of alpha-receptors produces peripheral vasoconstriction (pallor and hypertension) and urinary retention.
- Stimulation of beta-1 receptors increases myocardial contractility (inotropic effect) and heart rate (positive chronotropic effect).
- Stimulation of beta-2 receptors produces bronchodilatation and may be tremors.

A) Sympathomimetic beta adrenergic agonists

Mechanism of action

Stimulation of beta-adrenergic receptors of the bronchial smooth muscles will activate "adenylate cyclase enzyme". The enzyme is responsible for conversion of adenosine triphosphate (ATP) into cyclic adenosine monophosphate (cAMP), which is the biologically active substance responsible for bronchodilatation. Cyclic AMP is inactivated by "phosphodiesterase enzyme" to 5 adenosine monophosphate (5-AMP). This inactivation is blocked by methylxanthine derivatives (theophylline), which provide an alternative way of increasing the concentration of cAMP and bronchodilatation.

1. Nonselective agonists

These inotropic catecholamines are only used in acute severe asthma. Adrenaline is the mainly used drug. Isoproterenol infusion is currently not recommended because of the resultant marked tachycardia (See inotropic drugs).

- **Adrenaline: 0.01 mg/kg/dose ... ONLY subcutaneous.**

The dose may be repeated after 15 - 20 minutes, when necessary.

Adrenaline is used as an emergency drug to relieve severe bronchospasm in patients with acute severe allergic asthma. The therapeutic effect is rapid (within few minutes) and the duration of action is short. The main side effects are pallor (alpha effect), tachycardia (beta 1 effect) and may be tremors (beta 2 effect).

- Available preparation is:

R/ Adrenaline amp. (1 mg/ml).

Practical dosage is 0.1ml /kg of the diluted solution (1 ml + 9 ml saline).

2. Selective beta 2 agonists

These drugs produce a selective bronchodilatation without causing any cardiac effect. Another advantage over the nonselective drugs is their availability in oral and inhalation forms. They are mainly indicated in mild to moderate cases of acute asthma. These drugs have 2 main disadvantages

(a) They are not effective during the first 18 months of life because the beta 2 receptors are not yet well developed. However, they may have some effect if corticosteroids are concomitantly used.

(b) They are not suitable for long-term therapy in chronic asthma because of the rapid development of tachyphylaxis (tolerance or reduced effectiveness on prolonged use).

These drugs are generally safe in therapeutic dosage. Tremors usually occur with slight overdosage. Restlessness, headache and palpitation may also occur.

- **Salbutamol: 0.1 - 0.3 mg/kg/day ... oral.**
  0.1 - 0.2 mg (100-200 mcg)/dose ... inhalation.
  0.01 - 0.02 ml/kg/dose ... nebulization.

1. Oral forms: Suitable for all ages except infancy.

The daily dose (0.1 - 0.3 mg/kg/day) is divided into 3 - 4 doses.

RI Ventolin OR Vental syrup (2 mg/5 ml).
RI Salbulin OR Salbovent OR Salbutamol syrup (2 mg/5 ml) .
RI Ventolin OR Salbulin tablets (2 mg/5 ml).
RI Salbovent OR Brochovent tablets (2 mg).

Some preparations contain an expectorant as well.

RI Ventolin expectorant syrup (1 mg/5 ml + guaiphenesin).
RI Farcolin syrup (2 mg/5 ml + ammonium chloride).
RI Bronchovent syrup (2 mg/5 ml + guaiphenesin).

2. Inhalation forms: Suitable for children over 8 years.

The dose (0.1-0.2 mg/inhalation) is repeated 3 - 4 times daily.

RI Ventolin OR Vental inhaler (100 mcg/metered inhalation).
RI Ventolin Diskus (200 mcg/metered inhalation).

3. Nebulization form: Suitable for young children.

The calculated dose (0.01 - 0.02 ml/kg) is put in a nebulizer to be inhaled through a facemask. The dose can be repeated 3 - 4 times daily. Practically, 0.2 - 0.5 ml of the solution is added to 2 - 3 ml saline and is given by nebulization.

RI Ventolin OR Farcolin nebulizer solution (5 mg/ml).

- **Terbutaline: 0.1 - 0.2 mg/kg/day ... oral.**
  0.2 mg (200 mcg)/dose ... inhalation.

The daily dose is divided into 3 - 4 doses.

1. Oral forms: Suitable for children below 8 years.

RI Bricanyl syrup (1.5 mg/5 ml).
RI Aironyl syrup (1.5 mg/5 ml).
RI Bricanyl OR Aironyl tablets (2.5 mg).

Some preparations contain an expectorant or mucolytic as well:

RI Osipect syrup (1.5 mg/5 ml + guaiphenesin).
RI Cidopect syrup (1.5 mg/5 ml + guaiphenesin).
RI Bro-Zedex syrup (1.5 mg/5 ml + bromhexin).
RI All-Vent syrup (1.5 mg/5 ml + bromhexin).

2. Inhalation forms: Suitable for children over 8 years.

RI Bricanyl inhaler (200 mcg/metered inhalation).

- **Fenoterol: 0.1 - 0.2 mg/kg/day ... oral.**
  0.2 mg (200 mcg)/dose ... inhalation.

The daily dose is divided into 3 doses.

* Available preparations are:

RI Berotec syrup (2.5 mg/5 ml).
RI Berotec tablets (2.5 mg).
RI Berotec inhaler (200 mcg/metered inhalation).

B) Anticholinergic drugs

These drugs block the effect of acetylcholine at the post-ganglionic cholinergic endings (i.e. anti-acetylcholine) and also at the non-innervated receptors on the blood vessels (i.e. antimuscarinic). When these drugs are given by inhalation, they cause bronchodilatation without significant side effects.

- **Atropine: 0.02 - 0.05 mg/kg/dose ... nebulization.**

The dose can be repeated every 4 - 6 hours. Practically, 0.2 - 0.5 ml of the solution is added to 2-3 ml saline and is given by inhalation through a "nebulizer" and a facemask. At therapeutic dosage, the drug is safe in children.

The drug can be used in infants and young children with moderate to severe acute asthmatic attack when salbutamol nebulization is not available. Both drugs can be used in severe cases with better results than with either drug alone.

* Available preparation is:

RI Atropine sulphate amp. (1 mg/ml).

Inhalation through the mouth by an "inhaler"



Inhalation through the nose by a facemask and nebulizer



- **Ipratropium: 20 - 40 mcg/kg/dose ... inhalation.**

The dose can be repeated every 6 hours.

The drug is useful in cooperative children above the age of 8 years but the child should be trained how to use the inhaler. Compared to atropine, the drug has the advantages of prolonged action and the fewer side effects. The drug is recently available as nebulization solution to be used for young children. The dose is 0.5 - 1.0 ml of the drug added to 3 - 4 ml saline.

* Available preparations are:

RI Atrovent inhaler (20 mcg/metered inhalation).
RI Atrovent pediatric nebulization solution (250 mcg/2 ml).
RI Atrovent nebulization solution (500 mcg/2 ml).

* It is also available in combination with salbutamol.

RI Combivent inhaler (20 mcg + 100 mcg salbutamol /metered inhalation).
RI Combivent nebulization solution (250 mcg/2 ml).

C) Methylxanthine derivatives

Theophylline is an irritant, relatively insoluble drug. **Aminophylline** is a salt of theophylline with ethylenediamine. It is more soluble than theophylline, but still irritant drug, so, it can be only used I.V. and not I.M. or oral administration. **Acephylline** (Etaphylline) and **Dyphylline**, are less-irritant theophylline variants which are available in oral, rectal and parenteral forms.

The ***mode of action*** of theophylline as a bronchodilator is uncertain. It is no longer held that it is through phosphodiesterase inhibition. Other possible modes of action include adenosine antagonism, prostaglandin antagonism and enhancement of binding of cyclic AMP to a cyclic AMP binding protein. An effect on calcium flux across cell membrane may be also responsible.

The ***pharmacological effects*** of theophylline include bronchodilatation in addition to several important effects:

1. Mast cell stabilizing effect: Theophylline inhibits the release of chemical mediators from the mast cells so it is very useful in asthma prophylaxis.
2. Central respiratory stimulation: It stimulates the medullary respiratory centers.
3. Stimulant effect on respiratory musculature. It stimulates respiratory muscles and delays the occurrence of muscle fatigue, so, it is useful in chronic pulmonary conditions as bronchopulmonary dysplasia.
4. Increased myocardial contractility and heart rate.
5. CNS effects as irritability and sleeplessness may also occur.

- **Theophylline: 15 - 20 mg/kg/day ... I.V., oral or rectal.**

The daily dose is divided into 4 doses (every 6 hours). Maximum dosage is 600 mg/day. Therapeutic response is related to theophylline serum level. Therapeutic serum level is 10 - 20 mcg/ml.

* Available preparations are:

1. Parenteral forms: For slow I.V. injection over 10 minutes.

RI Minophylline N amp. (125 mg/5 ml).
RI Minophylline amp. (300 mg/2 ml).
RI Minophylline OR Etaphylline amp. (500 mg/5 ml).

Parenteral forms are used in acute severe asthma. The calculated dose (every 6 hours) can be given by continuous infusion. After initial response in 2 - 3 days, therapy can be continued with oral forms.

2. Oral forms: There are 2 types. The rapidly absorbed forms are suitable for short-term therapy of acute asthma and the slowly absorbed forms (sustained-release preparations) are suitable for long-term therapy of chronic asthma.

• The rapidly absorbed preparations, available in Egypt, are only those of acephylline. These preparations are only used in mild to moderate cases of acute asthma. Duration of therapy is 1 - 2 weeks.

RI Minophylline syrup (100 mg/5 ml).
RI Etaphylline syrup (100 mg/5 ml).
RI Amriphylline syrup (100 mg/5 ml).
RI Epicophylline with phenobarbitone syrup (100 mg/5 ml).
RI Epicophylline syrup (125 mg/5 ml).

Some oral preparations contain a mucolytic or expectorant as well:

RI Trisolvin syrup (50 mg/5 ml + ambroxol + guaiphenesin).
RI Farcosolvin syrup (50 mg/5 ml + ambroxol + guaiphenesin).
RI Tussipect-N syrup (50 mg/5 ml + guaiphenesin).
RI Neo-minophylline syrup (50 mg/5 ml + guaiphenesin).
RI Mucophylline syrup (100 mg/5 ml + bromhexin).

• The sustained-release preparations are suitable for long-term therapy in chronic asthma (See Asthma controllers and mast cell stabilizers).

3. Rectal forms are only those of acephylline. Absorption of rectal forms is erratic and unreliable, so, they are not recommended for regular use.

RI Etaphylline pediatric supp. (100 mg).
RI Amriphylline pediatric supp. (100 mg).
RI Minophylline pediatric supp. (125 mg).
RI Farcophylline pediatric supp. (125 mg).

Signs of theophylline toxicity

Early signs of overdosage or toxicity include irritability, sleeplessness and tachycardia. With serum level above 20 mcg/ml, signs of toxicity include vomiting, jitteriness and hyper-reflexia. The most serious signs of toxicity are cardiac arrhythmias and seizures.

With clinical suspicion, dosage should be lowered and serum theophylline level should be monitored. Therapeutic level is between 10 - 20 mcg/ml.

5. Asthma Protective Drugs (or Asthma Controllers)

Mast cell stabilizers	
Corticosteroids: Inhalation	100 mcg/dose ... inhalation ... 2-3 times daily.
Oral	2 mg/kg/day ... oral.
Salmeterol (long-acting β agonist):	25 - 50 mcg/dose... inhalation... 2 times daily
Cromolyn sodium:	5-20 mg/dose ... inhalation... 4 times daily.
Sustained-release theophylline:	15 - 20 mg/kg/day ... oral.
Ketotifen:	0.05 mg/kg/day ... oral.
Leukotriene modifiers	
Montelukast:	4 - 10 mg ... oral ... once daily every evening.

These drugs are mainly used as a long-term therapy in patients with ***persistent asthma*** where frequent or daily coughing and wheezing are present. It is important to emphasize that these drugs are not suitable for acute episodes of bronchospasm, where bronchodilator drugs (asthma relievers) should be used.

- **Mast cell stabilizers** are drugs that have a protective effect on mast cells. They prevent degranulation and release of the chemical mediators that result in bronchospasm and mucous membrane inflammatory changes.

- **Leukotriene modifiers** block leukotriene receptors and prevent the release of leukotriene LTD4, which is a potent asthmogenic mediator.

Recently, inhaled corticosteroids (ICS), long-acting β_2 agonist (LABA) and leukotriene modifiers (LMs) are the mainly used drugs.

A) Inhaled corticosteroids (ICS)

These drugs are recently considered the first-line drugs for choice.

- **Beclomethasone: 100 mcg/dose ... inhalation ... 3 times daily.**

The drug exerts a topical effect on the lungs without significant systemic absorption. Therapy can be continued for prolonged periods without side effects.

RI Becotide OR Beclosone inhaler (50 mcg/puff).
(Practical dosage: 2 puffs/dose, 3 times daily).

- **Budesinide: 100- 200 mcg/dose ... inhalation ... twice daily.**

It has the advantage of long duration of action and can be given twice daily.

RI Pulmicort Turbuhaler (100 mcg/puff).
RI Pulmicort Turbuhaler (200 mcg/puff).
(Practical dosage is one puff/dose ... twice daily).

- **Fluticasone: 50 -100 mcg/dose ... inhalation ... twice daily.**

It has the advantage of long duration of action and can be given twice daily.

RI Flixotide inhaler 50 (50 mcg/puff).
RI Flixotide inhaler 125 (125 mcg/puff).
RI Flixotide Diskus 50 (50 mcg/ metered inhalation).
RI Flixotide Diskus 100 (100 mcg/ metered inhalation).
RI Flixotide Diskus 250 (250 mcg/inhalation).
(Practical dosage is 1-2 inhalations/dose ... twice daily).

The Diskus form is more expensive than the inhaler form but it has the advantages of accurate dosage and the presence of a counter that counts the released doses. It usually contains 60 doses, sufficient for one-month use.

B) Long-acting β_2 agonist (LABA)

- **Salmeterol: 25 - 50 mcg/dose ... inhalation ... 2 times daily.**

Salmeterol is a long-acting selective beta 2 agonist with duration of action lasting for 12 hours. In addition to its bronchodilating effect, it has also a mast cell stabilizing action. It can be used as a single drug therapy or in addition to other drugs especially inhalation steroids. Tremors may occur with overdosage.
* Available preparations are:

RI Serevent OR Salmeterol inhaler (25 mcg/metered inhalation).
RI Serevent Diskus (50 mcg/metered inhalation).

- **Fluticasone +Salmeterol** (inhaled corticosteroids and long-acting beta 2 agonist) are recently available together in one preparation:

RI Seretide Diskus 100 (100 mcg fluticasone + 50 mcg salmeterol / inhalation).
RI Seretide Diskus 250 (250 mcg fluticasone + 50 mcg salmeterol / inhalation).
RI Seretide Diskus 500 (500 mcg fluticasone + 50 mcg salmeterol / inhalation).

C) Leukotriene modifiers (LMs)

- **Montelukast: 4 -10 mg ... oral ... once daily every evening.**

Montelukast ia a leukotriene-receptor blocker, which is used as an effective preventive agent in asthma. The drug prevents the release of leukotriene LTD4, which is a potent asthmogenic mediator. The main advantage of this drug is its availability in oral forms suitable for young children. It is given in a dose of 4-5 mg (one sachet or one tablet) daily in the evening. Adverse effects include headache, dizziness, dyspepsia and fatigue. The drug is very expensive.
* Available preparations are:

RI Singulair OR Kokast OR Clear Air chewable tablets for children (4 mg).
RI Singulair OR Montekal OR Idul Air chewable tablets for children (5 mg).
RI Singulair OR Montekal OR Clear Air OR Idul Air tablets (10 mg).

D) Other asthma controllers

- **Sustained-release theophylline: 15 - 20 mg/kg/day ... oral.**

The daily dose is divided into 2 doses (every 12 hours). The total daily dose should not exceed 600 mg. The main advantage of this drug is its availability as oral drug suitable for young children. The long-term therapy is guided with monitoring of theophylline serum level. Therapeutic response is usually achieved with serum level of 10 - 20 mcg/ml.

* Available preparations are:

RI Quibron S-R OR Minophylline S-R tablets (300 mg).
RI Theo S-R OR Theofar S-R capsules (100 mg), (200 mg) and (300 mg).
RI Vent-Retard capsules (100 mg) , (200 mg) and (300 mg).

(The tablet form can be divided into 2 or 3 portions)

- **Ketotifen: 0.05 mg/kg/day ... oral.**

The daily dose is divided into 2 doses (every 12 hours).

Ketotifen is an antihistamine with mast cell stabilizing activity. It can be tried in preschool children with mild persistent asthma. The main side effect is drowsiness due to its antihistaminic effect. Available preparations are:

RI Zaditen OR Prophallerge OR Ketoti OR Zylofen syrup (1 mg/5 ml).
RI Zaditen OR Prophallerge OR Ketoti OR Zylofen tablets (1 mg).

(Practical dosage is one teaspoonful /20 kg /day).

- **Cromolyn sodium: 5-20 mg/dose ... inhalation ... 4 times daily.**

Cromolyn sodium acts specifically as a mast cell stabilizer. It has no bronchodilator, anti-inflammatory or antihistaminic effect.

* Available preparations are:

RI Intal inhaler (5 mg/metered inhalation).
RI Intal nebulization solution (20 mg/2 ml ampoules).

- **Oral corticosteroids (prednisone or prednisolone): 2 mg/kg/day.**

The long-term use of oral corticosteroids in asthma should be restricted to severe cases of persistent asthma in which the above drugs are not effective.

Treatment should start with high dosage (2 mg/kg/day ... oral... in 4 divided doses) for about one week to achieve an adequate control. Regimen is then changed to the alternate-day therapy, where the total daily dose is given as a single dose in the morning every 48 hours (Every other morning therapy). Dosage is then gradually reduced (every week) to reach the lowest effective dosage (maintenance dose), which is usually 20 - 30 mg every other morning.

RI Predsol OR Xilone syrup (5 mg/5 ml).
RI Hostacortin OR Hostacortin-H tablets (5 mg).

6

Drugs of Digestive System

1. Antacids.
2. Antiemetic Drugs.
3. Spasmolytics.
4. Antidiarrheal Drugs.
5. Laxatives.

1. Drugs for Gastric Hyperacidity

Antacids (neutralize released acids)
Aluminium hydroxide gel

H_2 receptors antagonists (decrease HCl secretion)
Cemitidine
Ranitidine
Famotidine
Nizatidine

The last 3 drugs are more specific, more potent and with fewer side effects than cemitidine.

A) Antacids

Antacids are drugs that used to neutralize the gastric hydrochloric acid. The indications for use in pediatric practice are:

1. Gastroesophageal reflux (see neonatology).
2. Acute gastric ulceration (stress ulcers) especially in critically sick infants.
3. Peptic ulcer, which is not uncommon in older children.

Aluminium hydroxide gel is the mainly used drug. Several preparations are available in both syrup and tablet forms.

1. **Syrup form**: For infants and young children.
   RI Maalox OR Mucogel OR Epicogel suspension.
   RI Alkasilone OR Alkomag suspension.
   RI Gelcosicone OR Gelcocaine suspension.
2. **Tablet form:** For older children.
   RI Maalox chewable OR Rennie chewable tablets.
   RI Antacid chewable OR Acicone chewable tablets.
   RI Alkasilone OR Magsilon tablets.

* **Dosage:** It is 5 ml (one teaspoon) in infants and 10-15 ml (2-3 teaspoon) or one tablet in older children given with meals 3 - 4 times/day.

B) H_2 receptors antagonists

These drugs reduce the HCl secretion in the stomach. They are mainly used in the treatment of hyperacidity and peptic ulcer. Available preparations are:

- **Cemitidine:** ***RI Tagamet OR Cimetidine tablets (200 mg) and (400 mg).***
- **Ranitidine:** ***RI Zantac OR Ranitak tablets (150 mg) and (300 mg).***
- **Famotidine:** ***RI Famotine OR Antodine tablets (20 mg) and (40 mg).***
- **Nizatidine:** ***RI Nizatine OR Ulcfree capsules (150 mg) and (300 mg).***

* **Dosage:** It is usually one tablet or one capsule per day.

2. Antiemetic Drugs

Dopamine-receptor antagonists
Metoclopramide: 0.5 mg/kg/day ... oral, rectal, I.V. or I.M.
Domperidone: 1 mg/kg/day ... oral or rectal.
Chlorpromazine: 2 mg/kg/day ... oral.

Anticholinergic drugs
Belladonna extract.
Hyoscine or scopolamine.
Some antihistamines as promethazine.

A) Dopamine-receptor antagonists

These drugs produce their antiemetic effect through blocking dopamine-receptors of chemoreceptor trigger zone (CTZ) in medulla. Metoclopramide and domperidone have an additional antiemetic effect on the gut, while chlorpromazine has also an additional action through blocking the cholinergic receptors of vomiting center (VC) in medulla.

- **Metoclopramide: 0.5 mg/kg/day ... oral, rectal, I.V. or I.M.**

The daily dose is divided into 3 - 5 doses, given 30 minutes before feeding. The dose can be increased, in severe cases, up to 1.0 mg/kg/day.

Metoclopramide is the most commonly used antiemetic in pediatric practice. It is mainly indicated in 2 conditions:

1. Acute vomiting associated with acute infections especially severe cases of gastroenteritis.
2. Chronic regurgitation and vomiting associated with upper gastrointestinal dysfunctions especially gastroesophageal reflux in early infancy.

The antiemetic effect is through 2 mechanisms:

(a) Central, by blocking the dopamine receptors in chemoreceptor trigger zone.
(b) Peripheral, by its gastrokinetic effect. It raises the tone in the lower esophageal sphincter, relaxes the pyloric antrum and increases peristalsis and emptying of the upper gastrointestinal tract.

As the drug crosses the blood brain barrier, overdosage will induce extrapyramidal manifestations (torticollis, facial spasms and oculogyric crises). Antidote is promethazine (phenergan) or diphenhydramine (Benadryl).

* Available preparations are:

1. Ampoules: For I.V. or I.M. injections.

RI Primperan OR Meclopram OR Plasil amp. (10 mg/2 ml).

2. Tablets: For older children.

RI Primperan OR Meclopram OR Plasil tablets (10 mg).

3. Syrups: For children.

RI Primperan OR Meclopram OR Plasil syrup (5 mg/5 ml).
(Dosage is one teaspoon/10 kg/day ...divided).

4. Pediatric drops: For infants. The dosage varies with different preparations.

RI Primperan OR Meclopram drops (2.5 mg/ml = 0.15 mg/drop).
(Dosage is one drop/kg/dose ... oral ... 4 times/day).

RI Plasil drops (4 mg/ml = 0.2 mg/drop).
(Dosage is one drop/kg/dose ... oral ... 3 times/day).

5. Infantile suppositories: When oral intake is difficult.

RI Primperan OR Meclopram infantile supp. (10 mg).
(Dosage is one suppository/ 10 kg/day ... may be divided).

6. Adult suppositories: For older children.

RI Primperan OR Meclopram adult supp. (20 mg).
(Dosage is one suppository/ 10 kg/day ... may be divided).

- **Domperidone: 1.0 mg/kg/day ... oral or rectal.**

The daily dose is divided into 3 - 5 doses, given 30 minutes before feeding. The dose can be increased, in severe cases, up to 2 mg/kg/day.

The mechanism of action is similar to that of metoclopramide. It is used in both acute and chronic vomiting. It has the advantage of weak penetration across the blood brain barrier so overdosage is not associated with extrapyramidal manifestations. However, dosage should not be exceeded in infancy because blood-brain barrier is not yet well developed.

* Available preparations are:

RI Motilium OR Motinorm OR Dompidone suspension (5 mg/5 ml).
RI Gastromotil OR Farcotilium suspension (5 mg/5 ml).
RI Motilium OR Motinorm OR Dompidone supp. for infants (10 mg).
RI Motilium OR Motinorm OR Dompidone supp. for children (30 mg).
RI Motilium OR Motinorm OR Dompidone supp. for adults (60 mg).
RI Gastromotil supp. (10 mg), (30 mg) and (60 mg).
RI Motilium OR Motinorm OR Dompidone tablets (10 mg).
RI Gastromotil OR Farcotilium OR Synchro-Git tablets (10 mg).

- **Chlorpromazine: 2 mg/kg/day ... oral.**

The daily dose is divided into 3 - 5 doses, given 30 minutes before feeding.

The antiemetic effect is through two central mechanisms:

(a) Blocking the dopamine receptors in chemoreceptor trigger zone.
(b) Blocking the cholinergic receptors in vomiting center.

Although it is a highly effective drug, it is not used in modern practice because of its 2 major disadvantages:

(a) Strong sedating effect even in therapeutic dosage.
(b) Marked impairment of the consciousness and marked extrapyramidal manifestations with overdosage.

So, as the above 2 drugs (metoclopramide and domperidone) are always available, chlorpromazine is better to be avoided as antiemetic drug (see also psychotropic drugs).

* Available preparations are:

RI Neurazine drops (20 mg/ml = 1 mg/drop).

(Practical dosage is 2 drop/kg/day ... divided).

RI Neurazine OR Largactil OR Promacid tablets (25 mg).

B) Anticholinergic drugs

These drugs are rarely used in modern practice. However, **belladonna extract** and **homatropine** are commonly added in some antidiarrheal mixtures to act as a spasmolytic. **Promethazine** is not used as an antiemetic because of its strong sedating effect. However, it is particularly useful as an antidote in metoclopramide poisoning (see antihistamines).

3. Spasmolytics

Spasmolytic drugs		
Pipenzolate:	1.0	mg/kg/day ... oral.
Homatropine:	0.5	mg/kg/day ... oral.
Hyoscine:	0.5	mg/kg/day ... oral , rectal or parentral (I.V or I.M.).
Tiemonium:	1.0	mg/kg/day ... oral , rectal or parentral (I.V or I.M.).
Dicycolomine:	1.0	mg/kg/day ... oral.
Spasmolytic and analgesic combinations		

Mechanism of action and indications for use

Spasmolytics (antispasmodics) are anticholinergic drugs. They block the acetylcholine receptors in the gut leading to smooth muscle relaxation.

They are mainly indicated in the following conditions:

1. Infantile colic: Pipenzolate and homatropine are the mainly used drugs.
2. Recurrent abdominal pain: Hyoscine butylbromide and tiemonium are the mainly used drugs.
3. Renal colic due to ureteric spasm as in case of urinary stones.

A) Spasmolytic drugs

- **Pipenzolate: 1 mg/kg/day ... oral.**

The daily dose is divided into 3 - 5 doses, given 30 minutes before feeding. Pipenzolate is a synthetic anticholinergic drug, which is mainly used to relieve spasm of the gastrointestinal tract. **Infantile colic** is the main indication. However, it can be also used as an antiemetic through relieving pylorospasm and reducing tone and motility of the gastrointestinal tract.

The drug is available in form of pediatric drops suitable for neonates and young infants. Phenobarbital is included in the preparation to act as a sedative. Each 1 ml contains 4 mg pipenzolate and 6 mg phenobarbital.

* Available preparations are:

RI Spasmotal drops (4 mg + 6 mg/ml).
RI Babytal OR Piptal drops (4 mg + 6 mg/ml). | (1 ml = 30 drops).

(Practical dosage is 2 drops/kg/dose …3 – 4 times per day).

- **Homatropine: 0.5 mg/kg/day ... oral.**

The daily dose is divided into 3 - 5 doses, given 30 minutes before feeding. It can be used in infantile colic or in children with abdominal pain.

RI Novatropine drops (2 mg/ml).

(Practical dosage is one drop/kg/dose ... 3 - 4 times daily).

- **Hyoscine butylbromide: 0.5 mg/kg/day ... oral, rectal, I.V or I.M.**

  The daily dose is divided into 2 - 3 doses.
  It is particularly useful as an antispasmodic in children with recurrent abdominal pain. It is also used in renal colic due to ureteric spasms.
  Available preparations are:

  RI Buscopan syrup (5 mg/5 ml).
  RI Buscopan tablets (10 mg).
  RI Buscopan infantile supp. (7.5 mg).
  RI Buscopan ampoule. (20 mg /ml).

- **Tiemonium: 1 mg/kg/day ... oral, rectal, I.V or I.M.**

  The daily dose is divided into 3 - 4 doses. Available preparations are:

  RI Visceralgine syrup (10 mg/5 ml).
  RI Visceralgine Tablets (50 mg).
  RI Visceralgine supp. (20 mg).
  RI Visceralgine ampoule (5 mg/ ml).

- **Dicycolomine: 1 mg/kg/day ... oral or I.M.**

  The daily dose is divided into 3 - 4 doses. Available preparations are:

  RI Spasmorest syrup (10 mg/5 ml).
  RI Spasmorest tablets (10 mg) and (20 mg).
  RI Spasmorest ampoule (10mg/ ml).

B) Spasmolytic and analgesic combinations

These preparations are used in children with severe abdominal pain. During the episode, dosage can be roughly calculated as half to one tablet, one suppository (of the infantile form) or half to one suppository (of the adult form).
The dose can be repeated 2 - 3 times/day (when necessary).

- **Hyoscine butylbromide + metamizole:** Available preparations are:

  RI Buscopan compositum tablets (10 mg hyoscine + 250 mg metamizole).
  RI Buscopan compositum infantile supp. (7.5 mg + 300mg).
  RI Buscopan compositum adult supp. (10 mg + 1000 mg).

- **Camylofin + metamizole:** Available preparations are:

  RI Spasmopyralgin-M tablets (60 mg camylofin + 210 mg metamizole).
  RI Spasmopyralgin-M infantile supp. (20 mg + 250 mg).
  RI Spasmopyralgin-M adult supp. (40 mg + 500 mg).

- **Adiphenin + propyphenazone:** Available preparations are:

  RI Spasmin tablets (20 mg adiphenin + 220 mg propyphenazone).
  RI Spasmin infantile supp. (10 mg + 220 mg).
  RI Spasmin adult supp. (40 mg + 440 mg).

4. Antidiarrheal Drugs

Adsorbent powders

Kaolin:	No accurate dosage.
Pectin:	No accurate dosage.
Smectite:	No accurate dosage.

Antimotility drugs

Diphenoxylate:	0.5 mg/kg/day ... oral.
Loperamide:	0.2 mg/kg/day... oral.

Antisecretory drugs

Racecadotril:	1.5 mg/kg/dose... oral.

Antidiarrheal mixtures

Adsorbents, antimicrobial and spasmolytic mixtures.

Zinc supplementation

Oral zinc	10-20 mg/day ... for 10-14 days.

It is important to emphasize that the role of antidiarrheal drugs in management of acute gastroenteritis is minimal. In this condition, attention should be directed to 3 important aspects: (1) Preservation and restoration of fluid and electrolyte balance, (2) Dietetic management and (3) Specific antimicrobial therapy, when indicated.
(See management of acute gastroenteritis).

A) Adsorbent powders

These drugs have been thought to act by providing a protective coating on the intestinal mucosa and by adsorbing the toxic substances. However, they probably do not coat the bowel and the adsorption is not selective and is directed also to take up the non-toxic substances. Certainly, and whatever the mechanism of action, the therapeutic efficacy of these drugs is minimal, if at all.
* The available preparations are:

RI Kapect suspension OR Diastop suspension.
RI Smecta sachets OR Smecta suspension.

There is no accurate dosage of these preparations. Roughly, the dose is 3 - 4 teaspoons/day or half to one sachet, twice daily.

B) Antimotility drugs

Diphenoxylate and loperamide are opioids (morphine-related drugs) that produce their effect through inhibition of intestinal peristalsis. The mechanism of action is due to the direct effect on opioid receptors in the intestinal wall.

Although these drugs are generally effective, they are *absolutely contra-indicated* in acute gastroenteritis in infants and young children. Inhibition of peristalsis in these cases has many serious effects.

The main therapeutic indication of these drugs is the *chronic nonspecific diarrhea,* where careful inhibition of peristalsis may be useful.

- **Diphenoxylate: 0.5 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses.

Over-dosage is serious and should be avoided. It leads to paralytic ileus, CNS depression and respiratory depression. The action is antagonized by naloxone.

RI Lomotil liquid (2.5 mg/5 ml) and Lomotil tablets (2.5 mg).

(Practical dose is one teaspoon/5 kg/day ... divided).

- **Loperamide: 0.2 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses. Over-dosage is serious and produces the same effects of diphenoxylate (ileus, CNS and respiratory depression).

RI Loperazin OR Lopodium syrup (1 mg/5 ml) and capsules (2 mg).

(Practical dosage is one teaspoon/5 kg/day ... divided).

C) Antisecretory drugs

These drugs inhibit the intestinal hypersecretion induced by chemical or microbial agents, thus reducing the water and electrolyte losses.

- **Racecadotril: 1.5 mg/kg/dose ... oral ... 3 times per day.**

Racecadotril is an enkephalinase enzyme inhibitor (which is responsible for the degradation of endogenous enkephalines). Thus, it protects the endogenous enkephalines that act on enterocytes to prevent hypersecretion. The drug produces its antidiarrheal effect without slowing the gastrointestinal motility and without neurotoxicity (so it is better and safer than antimotility drugs). The drug can be used in *severe watery diarrhea* to decrease water and electrolyte losses.

RI Acetorphan sachets (30 mg/ sachet).

(Practical dose is half sachet/10 kg/dose ... 3 times per day for 3-4 days).

D) Antidiarrheal mixtures

There are several preparations marketed as antidiarrheal mixtures.

All preparations contain *adsorbent powders and antimicrobial drugs* as sulphonamide or a locally acting aminoglycoside (as neomycin, streptomycin or kanamycin). Some preparations contain also a *spasmolytic drug* as belladonna extract, homatropine or adiphenin. Bismuth salts are also added to some mixtures to act as *astringent.*

Although there is no scientific basis for use of these mixtures, they however may have some effect in mild to moderate cases of acute diarrhea. In severe cases, correction of fluid and electrolyte imbalance is of prime importance.

1. Mixtures of adsorbents and antimicrobials

RI Kapect compound suspension.
RI Diamycin suspension suspension.
RI Antinal OR Nifunal OR Diax suspension (200 mg /5 ml).
RI Antinal OR Nifunal OR Diax capsules (200 mg).

- Kapect compound suspension contains kaolin + pectin + co-trimoxazole.
- Diamycin suspension contains kaolin + pectin + neomycin + streptomycin + diiodohydroxyquinoline.
- Antinal, Nifunal and Diax contain nifuroxazide only.

2. Mixtures of adsorbents, antimicrobials and spasmolytics

RI Diakan-M suspension.
RI Enteroquin compound suspension.
RI Streptoquin suspension.

- Diakan contains kaolin + kanamycin + adiphenin + bismuth subcarbonate.
- Enteroquin compound contains kaolin and pectin + sulphonamide + diiodohydroxyquinoline + homatropine + bismuth carbonate.
- Streptoquin contains diiodohydroxqyuinoline + sulphonamide + streptomycin + homatropine.

(Choice between different preparations is not critical).

Dosage is roughly:

- One teaspoon, 3 times daily (in late infancy and early childhood).
- Two teaspoons, 3 times daily (in late childhood).

* Some preparations are available as packets to be dissolved in water.

RI Entocid OR Dysentrin packets.

- Entocid contains kaolin + pectin + sulphonamide + streptomycin.
- Dysentrin contains kaolin + pectin + sulphonamide + streptomycin.

* Other preparations are available in a tablet form for older children and adults.

RI Entocid OR Streptoquin OR Enteroquin tablets.

E) Zinc supplementation

Recently, it is recommended by WHO and UNICEF that all children with acute diarrhea in developing countries should receive oral zinc supplementation for 10-14 days (10-20 mg elemental zinc/day). There is strong evidence that zinc supplementation to children with diarrhea leads to reduced duration and severity of diarrhea and could prevent deaths. The mechanism of action is through antisecretory effect (by decreasing cAMP) and anti-infective effect (by direct inhibition of many enteric bacterial and viral pathogens).

RI Aqua Ream Z syrup (15 mg elemental zinc/5 ml).

5. Laxatives

Osmotic laxatives	
Magnesium hydroxide:	0.5 ml /kg/ dose ... oral.
Lactulose:	0.5 ml /kg /day ... oral.
Lactitolum:	5 - 10 gm/ dose ... oral.
Stimulants	
Sodium picosulphate:	0.3 mg/kg/dose ... oral.
Contact laxatives (suppositories or enema)	
Glycerine:	700 - 1400 mg ... when necessary.
Bisacodyl:	5 - 10 mg ... when necessary.
Sodium sulphate	

Lubricants and fecal softeners as liquid paraffin should be avoided in children because of the risk of lipid aspiration.

Laxatives are drugs commonly used in acute and chronic constipation. In acute constipation, intestinal obstruction should be always excluded before using these drugs. Also in chronic constipation, organic causes should be excluded before considering the case as a chronic dysfunctional constipation.

A) Osmotic laxatives

These drugs act through retaining water in the intestinal lumen by their osmotic effect, thus, interfering with its absorption. This will increase the bulk of intestinal movements and decrease the viscosity.

- **Magnesium hydroxide suspension (7.5%): 0.5 ml/kg/dose ... oral.**

The dose is usually given at night. It may be increased or decreased according to the individual response.

Magnesium hydroxide is a mild safe laxative that can be used even in infants. It is mainly used in chronic constipation.

* Available preparation is:

RI Laxomag suspension (7.5%).

(Dosage is one teaspoon/10 kg ... once at night).

- **Lactulose syrup (65%): 0.5 ml/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses.

Lactulose is a synthetic disaccharide, which is not absorbed and acts as an osmotic laxative. It is mainly used in chronic constipation.

It is also used in hepatic encephalopathy, where it reduces the formation and absorption of ammonia. The mechanism of action depends on fermentation of the drug in the colon to lactic and acetic acids. These acids will lower the pH in the colon, thus, inhibiting the growth of ammonia producing organisms and reducing the diffusion of ammonia from the colon to the blood.

* Available preparations are:

RI Lactulose OR Lactulax syrup.

RI Duphalac OR Sedalac OR Laxolac syrup.

(Practical dosage is one teaspoon/10 kg/day ... divided).

- **Lactitolum: 5 - 10 grams /day.**

The dose may be increased or decreased according to the response.

Lactitolum is a disaccharide, which is not absorbed by the gut and acts as a laxative (same mechanism of action of lactulose).

RI Importal sachets (10 grams).

(The sachet is dissolved in a half glass of water).

B) Stimulants

Stimulant drugs produce their effect through direct stimulation of the sensory endings in the colon, thus, helping evacuation.

- **Sodium picosulphate: 0.3 mg/kg/dose ... oral ... once at night.**

The dose may be increased or decreased according to the response. The drug is mainly used in chronic constipation.

* Available preparations are:

RI Picolax OR Normalax drops (7.5 mg / ml = 0.3 mg/drop).

RI Laxeol OR Skilax drops (7.5 mg / ml = 0.3 mg/drop).

(Practical dosage is one drop/kg/dose ...once at night).

RI Laxeol Tablets (10 mg).

C) Contact laxatives

These drugs cause local irritation of rectal mucosa, thus, stimulating evacuation. They are only used for temporary relief of acute constipation.

- **Glycerine: one suppository ... rectally ... when needed.**

* Available preparations are:

RI Glycerine infantile supp. (700 mg).

RI Glycerine adult supp. (1400 mg).

- **Bisacodyl: one suppository ... rectally ... when needed.**

* Available preparations are:

RI Bisadyl OR Abilaxine infantile supp. (5 mg).

RI Bisadyl OR Abilaxine adult supp. (10 mg).

The above three trade names are also available as tablets:

RI Bisadyl OR Abilaxine tablets (5 mg).

- **Sodium Phosphate: one enema... rectally ... when needed.**

* Available preparations are:

RI Enemax enema (100 ml).

7

Other Commonly Used Drugs

1. Antihistamines.
2. Hormonal Therapy.
3. Vitamin Therapy.
4. Mineral Therapy.
5. Cancer Chemotherapy.
6. Topical Medications.
7. Eye Medications.

1. Antihistamines

Highly sedating antihistamines	
Promethazine:	0.5 mg/kg/day ... oral.
Cyproheptadine:	0.2 mg/kg/day ... oral.
Moderately sedating antihistamines	
Clemastine:	0.05 mg/kg/day... oral.
Dimethindene:	0.05 mg/kg/day... oral.
Mequitazine:	0.25 mg/kg/day... oral.
Pheniramine:	1.0 mg/kg/day ... oral.
Non-sedating antihistamines	
Loratadine:	0.5 mg/kg/day ... oral.
Cetirizine:	0.5 mg/kg/day ... oral.
Ebastine:	0.5 mg/kg/day ... oral.

Histamine is a naturally occurring amine present mainly in mast cells of most body tissues. In case of allergy, there is an excessive release of histamine that leads to the known allergic manifestations (itching, flushing, wheal and flare and may be hypotension and shock).

The severity of the allergic condition depends on the amount and rate of histamine release. In acute severe conditions as anaphylaxis and serum sickness, the case may be rapidly fatal due to severe airway obstruction and severe shock.

Anti-allergy drugs or histamine antagonists

Anti-allergy drugs are the drugs that can oppose the effects of histamine. According to the mechanism of action, there are 3 groups:

1. Physiological antagonists: These drugs antagonize the effects of histamine by producing opposite effects. **Adrenaline** is the main physiological antagonist. It causes bronchodilatation and capillary vasoconstriction (opposite effects of histamine). It is used in emergency situations, where an immediate action is required. It is given subcutaneous in a dose of **0.01 mg/kg.**

2. Histamine-1 receptor antagonists (antihistamines): These drugs block histamine receptors and prevent histamine from reaching its sites of action. They are used in acute and chronic allergic conditions.

3. Corticosteroids: They stabilize mast cells and prevent the formation and release of histamine. They are used in severe acute conditions (with adrenaline) and in resistant chronic conditions (with antihistamines). See urticaria and atopic dermatitis.

A) Highly sedating antihistamines

These drugs have a strong sedating effect at therapeutic dosage so they are preferably used at night. When morning dose is required, it should be smaller than the evening dose.

- **Promethazine: 0.5 mg/kg/day ... oral.**

The daily dose is either given as a single night dose or divided into 2 unequal doses (1/3 in the morning and 2/3 in the evening). However, the sedating effect is transient and it usually disappears after few days of continuous use. At that moment, the 2 doses can be equal.

The main side effects, in addition to sedation, are the anticholinergic effects as dry mouth, dryness of bronchial secretions and difficult micturition.

Over-dosage leads to marked impairment of consciousness.

* Available preparations are:

RI Phenergan syrup (5 mg/5 ml).
RI Promantine syrup (5 mg/5 ml).

- **Cyproheptadine: 0.2 mg/kg/day ... oral.**

The daily dose is either given as a single night dose or divided into 2 unequal doses. (as promethazine).

The drug has an appetizing effect. However, it should not be used for that purpose.

* Available preparations are:

RI Triactin syrup (2 mg/5 ml).
RI Periactin syrup (2 mg/5 ml).
RI Triactin OR Cyptadine tablets (4 mg).

B) Moderately sedating antihistamines

- **Clemastine: 0.05 mg/kg/day ... oral.**

The daily dose is divided into 2 doses (morning and evening). The night dose is bigger than the morning dose.

* Available preparations are:

RI Tavegyl syrup (0.5 mg/5 ml).
RI Tavegyl tablets (1 mg).

- **Dimethindene: 0.05 mg/kg/day ... oral.**

The daily dose is divided into 2 - 3 doses.

* Available preparations are:

RI Fenistil drops (1 mg/ml = 0.05 mg/drop).
RI Fenistil syrup (0.5 mg/5 ml).
RI Fenistil tablets (1 mg).

- **Mequitazine: 0.25 mg/kg/day ... oral.**
  The daily dose is divided into 2 doses.

* Available preparations are:

RI Primalan syrup (2.5 mg/5 ml).
RI Primalan tablets (5 mg).

- **Pheniramine: 1.0 mg/kg/day ... oral.**
  The daily dose is divided into 2 - 3 doses.

* Available preparations are:

RI Avil syrup (10 mg/5 ml).

C) Non-sedating antihistamines

These drugs have a selective peripheral H_1 receptor antagonistic effect with almost absent central effect, so their action is not accompanied with sedation or impairment of the psychomotor skills or subjective feelings. They are suitable in allergic rhinitis, allergic conjunctivitis and chronic urticaria.
All these drugs are long-acting and are used as a single daily dose.

- **Loratadine: 0.5 mg/kg/day ... oral.**
  The daily dose is given as a single dose (long acting drug).

* Available preparations are:

RI Claritine syrup (5 mg/5 ml).
RI Mosedin OR Loratan syrup (5 mg/5 ml).
RI Claritine tablets (10 mg).
RI Mosedin OR Loratan tablets (10 mg).

- **Cetirizine: 0.5 mg/kg/day ... oral.**
  The daily dose is given as a single dose (long acting drug).

* Available preparations are:

RI Zyrtec drops (Dosage is … one drop/kg/day)
RI Zyrtec OR Histazine-1 syrup (5 mg/5 ml).
RI Cetrak OR Cetritin syrup (5 mg/5 ml).
RI Zyrtec OR Histazine-1 tablets (10 mg).
RI Cetrak OR Cetritin tablets (10 mg).

- **Ebastine: 0.5 mg/kg/day ... oral.**
  The daily dose is given as a single dose (long acting drug).

* Available preparations are:

RI Evastine syrup (5 mg/5 ml)
RI Evastine OR Kestine tablets (10 mg).
RI Astine OR Ebastel tablets (10 mg).

2. Hormonal Therapy

The commonly used hormones for **"replacement therapy"** in pediatrics are:

Thyroid hormone:	6 - 10 mcg/kg/day ... oral.
Insulin:	0.5 - 1.0 unit/kg/day ... subcutaneous.
Antidiuretic hormone:	2 - 15 mcg/day ... intranasal.
	0.1 - 0.2 mg/day ... oral.
Growth hormone:	0.05 - 0.1 unit/kg/day ... subcutaneous.

1. Thyroid hormone

Thyroid hormones are L-thyroxine (T_4) and liothyronine (T_3). Both are stored in the gland as thyroglobulin, from which enzymatic hydrolysis releases T_4 and little T_3 into the circulation. About 30 - 50% of released T_4 is de-iodinated to biologically active T_3. Differences between both hormones are in their potency and duration of action. Liothyronine (T_3) is 5 times as active as T_4 (100 mcg T_4 is equivalent to 20 mcg T_3). Liothyronine (T_3) is weakly bound to plasma proteins, so, it produces its maximum effect in 24 hours and its effect passes off in one week. L-thyroxine (T_4) is strongly bound to plasma proteins, so, it reaches its maximum effect in 2 weeks and its effect passes off in 2 - 3 weeks.

- **L-thyroxine: 10 - 15 mcg/kg/day ... oral (in neonatal period).**
  8 - 10 mcg/kg/day ... oral (in infancy).
  4 - 6 mcg/kg/day ... oral (in childhood).

The daily dose is given as a single dose.

L-thyroxine is the drug of choice for congenital and acquired hypothyroidism because it provides both T_4 and T_3 (30 - 50% of T_4 is de-iodinated to T_3). It can be also used in endemic goiter and goiter of puberty. With L-thyroxine therapy in hypothyroidism, the following points are important:

1. Initial response to therapy does not appear before 2 weeks of onset, and maximum response usually occurs after 6 weeks.
2. Signs of therapeutic response include: increased activity and alertness, improvement in skin colour and temperature and reversal of all symptoms and signs.
3. Signs of overdosage include irritability, restlessness, diarrhea and abdominal cramps. Tremors may also occur.
4. Serum level of T_4 and TSH should be checked, 4 - 6 weeks after initiation of therapy. Optimum dose is that, which brings serum level of T_4 to upper half of normal level and returns TSH level to normal values. Dosage is adjusted according to the response.
5. Treatment with L-thyroxine is life long.

* Available preparations are:

RI Eltroxin tablets (50 mcg).
RI Eltroxin tablets (100 mcg).

2. Insulin

Insulin is synthesized and stored in granules in beta islet cells of the pancreas. Daily secretion is about 30 - 40 unit. The main functions of insulin are:
1. Increased glucose uptake in the tissues and diminished breakdown of hepatic glycogen to glucose. Both effects will result in reduction of blood glucose level.
2. Increased transport of aminoacids and potassium into the cells. This explains why insulin is used in the treatment of hyperkalemia.

Insulin is the only effective drug in the management of juvenile diabetes (Type I diabetes). Oral hypoglycemic drugs, used in adults, are not useful in childhood diabetes. According to the onset and duration of action, insulin preparations are classified into 3 types:

Type	Onset	Peak	Duration	Route
Rapid-acting insulin	**1/2 - 1 h.**	**2 - 4 h.**	**6 - 8 h.**	**I.V., I.M. or S.C**
Intermediate-acting insulin	**1 - 2 h.**	**4 - 12 h.**	**24 h.**	**S.C. only**
Long-acting insulin	**4 - 8 h.**	**14 - 20 h.**	**24 - 36 h.**	**S.C. only**

A) Rapid-acting insulin is used in management of diabetic ketoacidosis and also in management of ordinary cases.

1. Ketoacidosis: Insulin is given by the *low-dose continuous I.V. Infusion method.* Insulin infusion is begun without a bolus at a rate of **0.1 unit/kg/hour,** until blood glucose level reaches 300 mg/dl, then, discontinue infusion and give insulin subcutaneous in a dose of **0.2 - 0.4 unit/kg,** every 6 - 8 hours for about 24 hours.

2. Management of ordinary case: The total daily dose of insulin is about **0.5-1 unit/kg/day.** One third of that dose is regular insulin and two-thirds is intermediate insulin. The daily dose is given as a single subcutaneous injection before breakfast.

* Available preparations of regular insulin are:

RI Actrapid human insulin (40 units/ml) and (100 units/ml).
RI Humulin-R human insulin (40 units/ml) and (100 units/ml).
RI Actrapid OR Humulin-R human insulin Pen fill (100 units/ml).
RI Actrapid Novolet Pens (100 units/ml).

B) Intermediate-acting insulin is used in management of ordinary cases of diabetes in combination with regular insulin. The total daily dose is given as 1/3 regular insulin and 2/3 intermediate insulin (See management of diabetes).

* Available preparations are:

  RI Monotard human insulin (40 units/ml) and (100 units/ml).
  RI Insulatard human insulin (40 units/ml) and (100 units/ml).
  RI Humulin-N human insulin (40 units/ml) and (100 units/ml).
  RI Humulin-N human insulin cartridge (100 units/ml).
  RI Insulatard human insulin Pen fill (100 units/ml).
  RI Insulatard human insulin Novolet Pens (100 units/ml).

3. Antidiuretic hormone

The antidiuretic hormone of posterior pituitary is responsible for water reabsorption in the distal tubule. In diabetes insipidus, antidiuretic hormone deficiency results in marked increase in free water excretion without concomitant electrolyte loss (Polyuria with low-specific gravity).

Available preparations of antidiuretic hormone are the natural hormone (vasopressin) and the synthetic analogue (desmopressin).

- **Vasopressin: 1 unit (0.2 ml) / dose ... I.M.**
  to be repeated every 2 - 3 days.

The dose may be gradually increased to **5 -10 units (1 - 2 ml)** according to the response.

Vasopressin is not used in modern medicine because it has 3 disadvantages:

1. Short duration of action (3 - 4 hours).
2. Vasopressor effect: Rise of blood pressure and contraction of smooth muscles leading to intestinal colic.
3. Repeated intramuscular injections, which are not suitable for chronic use.

* Available preparations are:

  RI Pitressin tannate amp. (5 IU/ml).

- **Desmopressin: 01- 0.2 mg ... oral ... once or twice daily.**

Desmopressin is a synthetic analogue of vasopressin. It is also called "1-**D**esamino-8-**D**-**A**rginine **V**asopressin" or **"DDAVP".** It is the only used anti-diuretic hormone in modern medicine as it has 3 advantages over vasopressin:

1. Long duration of action.
2. Very little pressor effect.
3. Easy administration.

The only disadvantage is the price (very expensive drug).

Desmopressin is also effective in management of nocturnal enuresis and haemophilia. Recently, desmopressin is considered as the drug of choice in management of nocturnal enuresis.

* Available preparations are:

RI Minirin tablets (0.1 mg).
RI Minirin tablets (0.2 mg).

With the solution form (which is the cheapest), a graduated tube is included for calculation of dosage and intranasal administration.

4. Growth hormone

Growth hormone is secreted by anterior lobe of the pituitary gland. It promotes growth and protein metabolism. In case of deficiency, growth failure and proportionate short stature will occur. Growth hormone is a "species specific", so, only the human growth hormone is effective in management of pituitary growth hormone deficiency.

- **Growth hormone: 0.05 - 0.1 unit/kg/day ... subcutaneous.**

Most patients show dramatic response in 6-12 months after initiation of therapy. Treatment should be continued for several years until closure of epiphyses occurs.

It is mainly used in growth hormone deficiency. However, it may be also indicated in case of intrauterine growth retardation with delayed bone age and failure to catch up.

* Available preparations are:

RI Norditropin vial (4 IU/ml).
RI Genotropin vial (4 IU/ml).
RI Somatropin vial (4 IU/ml).
RI Humatrope vial (4 IU/ml).
RI Norditropin vial (12 IU/ml).
RI Genotropin vial (16 IU/ml).

3. Vitamin Therapy

Fat-soluble vitamins

Vitamin A:	5000 – 1000 I.U/day... oral.
Vitamin D:	3000 – 5000 I.U/day... oral.
Vitamin E:	10 – 20 mg/day... oral.
Vitamin K:	10 – 20 mg/ ... oral, I.V. or I.M.

Water-Soluble vitamins

Vitamin B group:	B_1 (5 mg), B_2 (5 mg) and B_6 (5 mg)/ day ... oral.
Vitamin C:	100 – 200 mg/day ... oral.

Vitamin requirements and dietary sources

Vitamins are essential substances for metabolism that cannot be synthesized by the body and should be supplied in the diet. An exception is the formation of vitamin D_3 by the skin.

Vitamin	Requirements	Dietary sources
Vitamin A	2000 - 3000 I.U.	Whole milk, liver, egg yolk. Fresh fruits, green vegetables.
Vitamin D	400 I.U.	Fortified formulas, egg yolk.
Vitamin E	15 mg.	Green vegetables, oils of seeds.
Vitamin K	1 mg.	Green vegetables.
Vitamin C	50 mg.	Fresh fruits, green vegetables.
Vitamin B complex		Milk, meat, liver, whole grains, and green vegetables.
B_1 (thiamine)	1 mg.	
B_2 (riboflavin)	1 mg.	
B_6 (pyridoxine)	1 mg.	
B_7 (niacin)	10 mg.	
B_{12} (scopolamine)	2 mcg.	
Folic acid	150 mcg.	

It is important to know that any child who has at least one well-balanced meal a day and [illegible] minutes of play in sunshine is very unlikely to develop vitamin deficiency.

Vitamins are one of the most abused drugs in medicine. In many occasions, vitamins are prescribed to children who do not need them. Unfortunately, there is a strong belief among most people and many physicians that sub-clinical vitamin deficiencies are a cause of chronic ill health and liability to infections. On that assumption, many physicians continue to prescribe vitamins for vague unscientific reasons as "to increase appetite", "for good health" or "to protect against infections". Other physicians may yield to parental pressure and prescribe vitamins "on request". **Vitamins should be only prescribed for clear scientific reasons.** Indications can be classified as prophylactic and therapeutic.

A) Prophylactic vitamin therapy

• **Vitamin K_1 (1 mg ... I.M ... once)** is given at birth to prevent hemorrhagic disease of the newborn.

* Available preparations are:

RI Konakion amp. (10 mg/1 ml).
RI Haemakion amp. (10 mg/1 ml).

A pediatric form of vitamin K_1 is available and could be used by oral, I.M. or I.V. route. For oral use, the contents of the ampoule (0.2 ml) is withdrawn by a syringe and administered directly from the syringe into the baby's mouth.

RI Konakion MM pediatric amp. (2 mg/0.2 ml).

• **Vitamin C (25 - 35 mg/day ... oral)** is given to breast-fed infants during the first 2 months after birth to compensate for the deficient vitamin C in breast milk. At the age of two months, fresh sources of vitamin C (as orange juice, 30 - 50 ml/day) can replace the vitamin C drops. Available preparations are:

RI Cevilene drops (100 mg/ml = 5 mg/drop).
RI Vitamin C drops (100 mg/ml = 5 mg/drop).

(Practical dosage is 5 - 7 drops ... once daily ... up to the age of 2 months).

• **Vitamin D (400 IU/day ... oral)** is prescribed to dark coloured breast-fed infants at the age of 3 - 4 months to compensate for the deficient vitamin D in breast milk, and is continued till the infant is able to tolerate foods rich in vitamin D as egg yolk and meat (usually at the age of 7 - 10 months).

* Available preparations are:

RI Vitamin D_3 drops (100 IU/drop = 400 IU/4 drops).
RI Vidrop drops (100 IU/drop = 400 IU/4 drops).
(Practical dosage is 4 drops ... once daily).

* Vitamin D is also available in combination with calcium:

RI Pedical syrup (400 IU vitamin D + 50 mg Calcium /5 ml).
RI Calcid B12 syrup (400 IU vitamin D + 50 mg Calcium /5 ml).
RI Cal-D-B12 syrup (400 IU vitamin D + 50 mg Calcium /5 ml).

• **Vitamin B complex (in doses equal to daily requirements)** may be prescribed to febrile patients receiving oral antibiotic therapy to compensate for the decreased synthesis and increased demands. It is also indicated in patients on I.V. fluid therapy for more than three days.

• Available preparations of vitamin B complex contain vitamin C as well.

RI Beco-C OR Ecaplex-C OR Varolex-C syrup.
RI Vicibex OR Medivit OR Fortevit syrup.
(Practical dosage: One teaspoon (5 ml)/day ... oral).

• **All vitamins** are prescribed to patients with intestinal malabsorption and chronic diarrhea to compensate for the decreased intestinal absorption. They are also indicated in case of chronic liver diseases (defective utilization).

• Available multivitamin preparations (A + B + C + D) are:

1. Drops: *RI Bebe-vit drops.*
RI Enfa-vit drops.
RI Polyvit OR Polyvital drops.
RI Poly-Vi-Sol drops OR Abidec drops.
(Practical dosage: 5 -10 drops /day … oral).

2. Syrups: *RI Vitam syrup.*
RI Multi-Sanostol OR Multi-Vitol Forte syrup.
RI Provit OR Mixavit OR Elbavit OR Totavit syrup.
RI Fruital OR Alvital OR Polyvital syrup.
RI Theragran syrup.
(Practical dosage: One teaspoon (5 ml)/day ... oral.).

3. Chewable tablets: *RI Chewa-vit OR Child-vit chewable tablets.*
RI Pedia-vit OR Children chewable tablets.
RI Junior's chewable tablets.
(Practical dosage: One to two tablets/day ... oral.).

B) Therapeutic vitamin therapy

1. Single vitamin deficiency

• **Vitamin D deficiency:** It is common in late infancy due to prolonged breast-feeding which leads to "vitamin D deficiency rickets". Vitamin D is a group of fat-soluble sterols, which are responsible for calcium and phosphorus absorption from the gut and deposition of calcium and phosphorus in bones.

Vitamin D_3 (cholecalciferol) is formed in the skin by ultraviolet irradiation of 7-dehydrocholesterol. Vitamin D_2 (calciferol) is usually supplied in the diet and absorbed from the gut. Both forms (D_3 and D_2) are converted in the liver to 25-hydroxy vitamin D, and then in the kidney to 1, 25-dihydroxycholecalciferol, which is the active form of vitamin D.

The dose of vitamin D depends on the preparation used:

- **Vitamin D_3: 3000 - 5000 IU/Day ... oral ... for 3 weeks OR**
  600.000 IU/dose ... I.M. ... once.

(In vitamin D resistant rickets the dose is increased to 20.000 IU/kg/day).

* Available preparations of vitamin D_3 are:

1. Syrups: ***Rl Decal B_{12} syrup (1000 unit of vitamin D_3/5 ml).***
Rl Vitacal syrup (1000 unit of vitamin D_3/5 ml).
Rl Calci-cal syrup (1000 unit of vitamin D_3/5 ml).

(The above 3 preparations are identical. Each 5 ml contains 1000 units of vitamin D3 + 50 mg calcium + 10 mcg vitamin B12). Practical dosage is:
1-2 teaspoons (5-10 ml) ... 3 times daily ... For 3 weeks.

2. I.M ampoules: ***Rl Devarol-S amp. (600.000 unit of vitamin D_3/ml).***

- **One alpha hydroxycholecalciferol: 0.05 mcg/kg/day... oral.**

The drug, which is also called alphacalcidol, is converted in the liver to the active form of vitamin D (1,25 dihydroxycholecalciferol). It is mainly indicated for treatment of vitamin D resistant rickets of renal origin as hypophosphatemic vitamin D resistant rickets.

* Available preparation is:

Rl One Alpha drops (0.1 microgram/drop).
(Practical dosage is one drop/2 kg/day ... oral).

* ***Precaution:*** With prolonged vitamin D therapy, serum calcium level should be checked and it should not exceed 11 mg/dl.

* ***Vitamin D intoxication*** is much more serious than rickets. Early clinical manifestations include anorexia, irritability, constipation and polyuria. In case of suspicion, serum calcium level should be checked (hypercalcemia) and vitamin D should be discontinued. Oral steroids are given to reduce calcium absorption from the gut. Diet should be free of milk to reduce the calcium intake. It is important to remember that toxicity may persist for several weeks because of the large vitamin D stores in adipose tissue, so treatment should be continued till serum calcium is constantly within normal levels (9 -11 mg/dl).

- **Vitamin A deficiency:** Isolated vitamin A deficiency is uncommon. Clinical manifestations of deficiency include night blindness, xerophthalmia and hyperkeratinization of the skin.

Vitamin A is essential for the integrity of the epithelial tissue, but extra doses are not useful for increasing resistance to colds or other infections.

* The dose of vitamin A depends on the indication:

- Xerophthalmia: **100.000 I.U/day ... I.M. ... for 5 days.**
  Then: 25.000 I.U/day ... oral ... for 2 weeks.

- Night blindness or hyperkeratinization of the skin:

5000 - 10.000 IU/day ... oral ... for 2 weeks.

* Available preparations are:

RI A-Viton amp. (100.000 IU/ml).
RI Vitamin A capsules (25.000 IU).
RI A-Viton capsules (50.000 IU).

* It is also available with multivitamin preparations as:

RI Theragran liquid (10.000 IU/5 ml).
RI Fruital syrup (5.000 IU/5 ml).

Prolonged vitamin A therapy at high doses is toxic. It leads to anorexia, drying and cracking of the skin, hair loss, pain and swelling of long bones and increased intracranial pressure (pseudotumour cerebri).

- **Vitamin K deficiency:** it may occur with salicylate poisoning, prolonged antibiotic therapy and prolonged fasting especially with severe gastroenteritis or with chronic malabsorption. Clinical manifestations include bleeding from puncture sites or gastrointestinal bleeding. Vitamin K_1 is more effective, its action is rapid and more prolonged than other vitamin K preparations.

The dose is **5-10 mg ... I.V. , I.M. or oral** (with pediatric form).

* Available preparations are:

RI Konakion OR Haemakion amp. (10 mg/ml).
RI Konakion MM pediatric amp. (2 mg/0.2 ml).

- **Vitamin C deficiency:** Isolated vitamin C deficiency leads to scurvy, which may occur if fresh sources of vitamin C as orange juice are not offered to the infant. Early clinical manifestations include irritability, anorexia and generalized bony tenderness. With clinical suspicion, vitamin C drops are given in a dose of **100-200 mg/day ... oral.**

Fortunately, vitamin C is not toxic and any excess amounts will be excreted in urine. It is important to emphasize that large doses of vitamin C are not useful for prevention or treatment of common cold.

* Available preparations are:

RI Cevilene drops (100 mg/ml = 5 mg/drop).
RI Vitamin C drops (100 mg/ml = 5 mg/drop).
(Practical dosage is 10 drops, 3 times daily)

RI Vit-C 500 chewable tablets (500 mg).
RI Upsa- C effervescent tablets (500 mg).
RI Cevarol tablets (500 mg).
RI Vitacid C OR Amovit -C effervescent tablets (1000 mg).

- **Vitamin B deficiency:** Clinical deficiency of several components of vitamin B complex is very common in severe kwashiorkor. However, manifestations of other vitamin deficiencies are commonly present.

* Available preparations of vitamin B complex contain vitamin C as well.

RI Beco-C OR Ecaplex-C OR Varolex-C OR Vicibex OR Medivit syrup.

(Practical Dosage is one teaspoon (5 ml) ... 2 - 3 times per day).

2. Multiple vitamin deficiencies

It is present in severe kwashiorkor (diminished intake), chronic diarrhea and malabsorption (defective absorption), chronic liver disease (defective utilization), and chronic infection or inflammation (increased demands).

Composition of multivitamin preparations

Preparation		A	D	C	E	B complex				
		IU	IU	mg	mg	B1 mg	B2 mg	B6 mg	B7 mg	B12 mcg
Drops (per ml)	*Bebe-vit*	1500	400	40	5	0.5	0.6	0.6	8	—
	Enfa-vit	1500	400	35	5	0.5	0.6	0.4	8	2
	Polyvit	1000	2000	30	3	2	1	3	20	—
	Polyvital	5000	300	60	2.5	1.5	1.7	2.2	19	—
	Poly-Vi-Sol	3000	750	50	—	4	3	1	4	—
	Abidec	4000	400	50	—	1	0.4	0.5	5	—
Syrups (per 5 ml)	*Multi-Sanostol*	1200	100	50	1	1	1	0.5	5	—
	Provit	1200	100	50	1	1	1	0.5	5	—
	Alvital	1200	100	50	1	1	1	2	5	—
	Totavit	1200	100	50	1	0.7	0.7	0.5	5	2.5
	Vitam	1250	200	20	5	0.35	0.4	0.35	4.5	1.5
	Mixavit	5000	500	50	—	5	2	6	20	6
	Polyvital	5000	400	50	1	2	1	1	20	—
	Fruital	5000	1000	50	2.5	1.5	1.5	1	125	—
	Theragran	10000	400	200	—	10	10	4	100	5
Chewable Tablets	*Chewa-Vit*	2500	500	50	—	1	1.5	1	10	—
	Child-vit	4000	400	60	34	2	2.4	2	10	10
	Junior's	2500	400	60	15	1	1.2	1	13.5	4.5
Capsules	*Supravit*	2000	200	50	10	15	3	2	15	5
	Servivit Plus	5000	400	60	10	2	2	1	20	3
	Vitop	10000	1000	75	5	5	5	0.5	25	1

*** Note: The concentration of vitamins is not the same in different preparations.**

- Vitamin A concentration is low in some preparations (Multi-sanostol, Provit, Alvital, Totavit and Vitam syrups) and high in other preparations (Mixavit, Polyvital, Fruital and Theragran syrups).
- Vitamin D is low in most preparations except Fruital syrup (1000 IU/5 ml).

4. Mineral Therapy

Calcium:	100 - 200 mg/kg ... slow I.V 40 - 80 mg/kg/day ... oral.
Magnesium:	100 mg/kg ... slow I.V or I.M 2 - 5 ml/day ... oral.
Potassium:	20 - 35 mEq/liter ... I.V 2 - 4 mEq/kg/day ... oral.
Iron:	10 - 15 mg/day ... oral (prophylaxis) 6 mg/kg/day ... oral (therapeutic)

Minerals account for about 4% of body weight, which must be supplied in the diet. Although minerals do not provide energy, they are essential for several metabolic functions.

According to their amount in the body, minerals are classified into:

A) Macro-elements

1. Minerals in the skeleton

- **Calcium:** 99% in bones and teeth and 1% in blood plasma and body cells.
- **Phosphorus:** 85% in bones and 15% in all body cells.
- **Magnesium:** 70% in bones and 30% in red cells and various tissues.

2. Minerals dissolved in cellular fluids

- **Sodium:** 2/3 in extracellular fluid and 1/3 in the skeleton.
- **Potassium:** Inside the cells to balance the sodium outside.
- **Chloride:** Mainly in extracellular fluids and gastric juice.

(See I.V. fluid therapy).

B) Trace elements

1. Essential trace elements

- **Iron:** 70% in hemoglobin and 30% in myoglobin and various organs.
- **Zinc:** In all living tissues and component of 8 enzymes.
- **Iodine:** In thyroid gland.

2. Other trace elements

- **Considered essential:** Copper, Cobalt, Chromium, Manganese, Flourine and Selenium.
- **With known value:** Arsenic, Barium, Bromide, Cadmium, Nickel and Vanadium.
- **With unknown value:** Gold, Silver, Lead, Aluminium, Tin and Bismuth.

1. Calcium Therapy

Calcium is one of the 4 cations of the body (Ca^{++}, Mg^{+}, Na^{+}, K^{+}).

The normal daily requirements is about 0.5 - 1 gm. Calcium is incompletely absorbed from the gut (30% absorbed and 70% excreted in feces).

The normal serum calcium level is 9 - 11 mg/dl. It is present in 2 forms:

1. **Ionized calcium:** About 60% of total serum calcium.
2. **Non-ionized calcium**: About 40%, bound mainly to albumin and globulin.

The normal serum calcium level is under several regulatory mechanisms:

(a) Vitamin D: It increases calcium absorption from the gut and mobilizes calcium from blood to bones.

(b) Parathormone: It increases calcium reabsorption through renal tubules and mobilizes calcium from bones to blood.

(c) Electrolytes and acid base balance: Hypernatremia, hypokalemia or alkalosis leads to decreased level of ionized calcium.

99% of body calcium is present in bones and teeth. The remaining 1% has several important functions; neuromuscular irritability, blood coagulation, cardiac action and milk production.

(a) I.V calcium therapy

It is indicated in neonatal convulsions (hypocalcemic) and in hypocalcemic tetany.

The dose is **100 - 200 mg/kg ... I.V. over 5 minutes.** The dose can be repeated after 15 minutes, when necessary.

Some points are practically important:

(a) It is better to be diluted with saline, but don't add to solutions containing sodium bicarbonate (precipitation).

(b) Monitoring of the heart during injection is essential. Discontinue injection if bradycardia occurs.

(c) Don't use with digitalis (toxicity).

* Available preparation is:

RI Calcium gluconate amp. (1 gm/10 ml = 100 mg/ml).

(Practical dose is 1 - 2 ml/kg ... I.V... over 5 minutes).

Notice: Each 1 ml of calcium gluconate (10%) contains 9.3 mg elemental calcium. The dose of elemental calcium is 10- 20 mg/kg ... i.e. 1 - 2 ml/kg.

(b) Oral calcium therapy

It is indicated in hypocalcemic states as severe vitamin D deficiency rickets especially following I.V. calcium therapy for tetany. It is also indicated in hypoparathyroidism, chronic malabsorption and chronic renal failure.

The dose of elemental calcium is **40 - 80 mg/kg/day ... oral**. The daily dose is divided into 2 - 3 doses.

* Available preparations are:

  Rl Vi-Sol Ca syrup OR Pedical syrup (50 mg elemental Ca/5 ml).
  R Cal-D-B_{12} syrup OR Calcid B_{12} syrup (50 mg elemental Ca/5 ml).
  Rl Hi-Cal syrup (78 mg elemental Ca/5 ml).
  Rl Calcium sandoz syrup (110 mg elemental Ca/5 ml).
  Rl Calcium natural syrup (110 mg elemental Ca/5 ml).
  Rl Hi-Cal forte syrup (115 mg elemental Ca/5 ml).
  Rl Maxical-D suspension (150 mg elemental Ca/5 ml).
  Rl Calcium effervescent sachets (500 mg).
  Rl Calcichew chewable tablets (500 mg).
  Rl Novo- Calcium OR Fem-Cal 500 tablets (500 mg).
  Rl Calci- Max OR Maxi-Cal tablets (600 mg).

Practical dosage is different with the various preparations. Overdosage is not serious, because toxicity following oral administration does not occur.

2. Magnesium therapy

Magnesium is one of the 4 cations of the body. Normal daily requirements are about 500 mg. and normal serum level is 1.5 - 2.5 mEq/liter.

70% of body magnesium is present in bones and teeth. The remaining 30% are distributed in all body tissues. It is the principal cation of soft tissues, located chiefly intracellular. It is important for neuromuscular irritability and activation of enzymes of carbohydrate metabolism.

(a) I.V. or I.M. magnesium therapy

It is used in neonatal convulsions (hypomagnesemic) and in hypomagnesemic tetany. The diagnosis should be considered in every case of tetany not responding to I.V. calcium therapy.

The dose is **100 mg/kg ... slow I.V. or deep I.M.**

(The I.V. injection should be given in the side tube of I.V. line).

* Available preparations are:

  Rl Magnesium sulphate 50% (5 gm/10 ml = 500 mg/ml).
  Rl Magnesium sulphate 10% (1 gm/10 ml = 100 mg/ml).

Practical dosage is - 0.2 ml/kg (of the 50% preparation).
- 1.0 ml/kg (of the 10% preparation).

(b) Oral magnesium therapy

It is indicated in chronic constipation and in severe kwashiorkor. The dose of the magnesium hydroxide suspension (7.5%) is **2 - 5 ml/day ... oral.**

* Available preparation is:

  Rl Laxomag suspension (7.5%).

3. Potassium therapy

Potassium is one of the 4 cations of the body. It is present mainly as an intracellular ion (K+) to balance the extracellular sodium.

The normal daily requirements are about 2 mEq/kg.

The normal serum level is 4 - 5.6 mEq/liter.

Values up to 6.5 mEq/liter are normal in newborns.

Potassium is important for muscle contraction, nerve impulse conduction, heart rhythm and intracellular osmotic pressure and fluid balance.

Hypokalemia (serum level below 3 mEq/liter) occurs in severe diarrhea with dehydration, diabetic ketoacidosis, acute hepatic failure, severe kwashiorkor and with drugs as diuretics and corticosteroids. Clinical manifestations include muscle weakness, abdominal distension, tachycardia, drowsiness and confusion.

Hyperkalemia (serum level above 7 mEq/liter) occurs in acute renal failure, suprarenal failure and excessive intake of potassium-containing salts (iatrogenic). The most serious clinical manifestation is heart block, which occurs with serum level of 10 mEq/liter.

(a) I.V. potassium therapy

It is indicated in acute severe cases as severe dehydration, diabetic ketoacidosis and acute hepatic failure.

The concentration of potassium in I.V. solution should not exceed **35 - 40 mEq/liter.**

For details of therapy, see I.V. fluid therapy.

(b) Oral potassium therapy

It is indicated in severe kwashiorkor, convalescent cases of severe gastroenteritis and dehydration and with drugs as diuretics and corticosteroids.

The **dose is 2 - 4 mEq/kg/day ... oral.** The daily dose is divided into 2 -3 doses.

Fresh orange or tomato juice contains about 50 mEq/liter of potassium. These juices could be used for correction of mild cases. In severe cases, oral potassium salts are necessary.

* Available preparations are:

RI K-chlor syrup 6% (4 mEq/5 ml).

RI Potassium syrup 15% (10 mEq/5 ml).

Notice: K-chlor syrup contains potassium chloride, while potassium syrup contains potassium gluconate.

4. Iron therapy

Iron is an essential trace element. 70% of the body iron is present in hemoglobin and 30% in myoglobin and various organs.

The normal daily requirements are 10 - 15 mg/day. Foods rich in iron are egg yolk, meat, liver, whole grains and legumes.

The normal serum iron level is 90 - 150 mcg/dl.

Iron is absorbed from the gut (in ferrous form) according to body needs and is transported in plasma (in ferric form) bound to transferrin, which is a beta globulin. It is stored in liver, spleen, bone marrow and kidney as ferritin and hemosiderin to be carefully converted and reused.

(a) Prophylactic iron therapy

It is indicated in breast fed infants from the third or fourth month to compensate for the deficient iron in breast milk. As fresh cow milk is also deficient in iron, infants receiving fresh cow milk need also iron supplementation. Dried milk formulas are fortified with iron, so artificially fed infants do not need iron supplementation.

Treatment should be continued till the infant is able to tolerate foods rich in iron as egg yolk and meat (usually at the age of 7 - 10 months).

The dose is **10 - 15 mg of elemental iron/day ... oral.**

* Available preparations are:

RI Fer-in-sol drops. (15 mg elemental iron/0.6 ml).
RI Ferro-Z syrup (8 mg elemental iron/5 ml).

(Practical dosage is one dropper or one teaspoon... oral ... once daily).

* **Notice:** Parents should be oriented that iron therapy leads to darkening of the tongue and blackening of the stool. It is recommended to rinse the mouth after the daily dose to prevent darkening of the tongue.

(b) Therapeutic iron therapy

* Indications: It is indicated for treatment of iron deficiency anemia. Prolonged breast- feeding without supplementation is a common cause of iron deficiency anemia in late infancy (after the age of 9 months). Repeated blood loss, malnutrition and chronic diarrhea are also common causes.

* Dosage: The dose is **6 mg elemental iron/kg/day ... oral.** The daily dose is divided into 2-3 doses, between meals.

* Duration: Treatment should be continued for, at least, 2 -3 months. The first 2 - 3 weeks are to correct the anemia and the next 1-2 months are for repletion of iron stores in the liver, spleen and bone marrow.

* Response: The response to iron therapy is rapid. The appetite increases after 24 hours, and within 2-3 days, the reticulocytic count increases. From the 4th day onwards, a steady rise of hemoglobin level occurs, which may be up to 0.5 gm/day.

- Failure of response to iron therapy should suggest one of several possibilities. Poor absorption due to diarrhea, continued blood loss or associated

infection may be responsible. After exclusion of these possibilities, other causes of hypochromic microcytic anemia, especially thalassemia minor should be excluded (see Pediatric Clinical Diagnosis).

* Available preparations are with different iron concentration:

1. Syrups:

RI Ferromix OR KG.Ron syrup (15 mg elemental iron/5 ml).
RI Sytron syrup (27.5 mg elemental iron/5 ml).
RI Ferronil syrup (30 mg elemental iron/5 ml).
RI Vitaferrol OR Rubraton-B Elixir (38 mg elemental iron/5 ml).
RI Ferose syrup (50 mg elemental iron/5 ml).

2. Tablets and capsules:

RI Theregran-H tablets (66.7 mg elemental iron).
RI Ferose tablets (100 mg elemental iron).
RI Fesovit capsules (150 mg elemental iron).
RI Fumiron plus capsules (200 mg elemental iron).
RI Haema-caps OR Haematon capsules (350 mg elemental iron).

3. I.M ampoules: *RI Iron Dextran amp. (250 mg/5 ml).*

4. I.V ampoules: *RI Ferosac I.V ampoules (100 mg/5 ml).*

In case of severe anemia (hemoglobin level below 5 gm/dl), initial **packed red cell transfusion (5 ml/kg)** is indicated. It is important to remember that each 100 ml of blood provide 45 mg elemental iron.

Acute iron toxicity

Preparations containing iron should be kept out of reach of children. Accidental ingestion of 60 mg elemental iron/kg is toxic and may be fatal. Clinical manifestations of acute toxicity include vomiting, diarrhea, hematemesis and abdominal pain. Hypoglycemia and metabolic acidosis may occur 12 hours after ingestion. Severe hepatic necrosis with elevation of SGOT, SGPT and bilirubin may occur 2 - 4 days later. Treatment includes the following:

1. **Immediate stomach wash** with saline is important.
2. **Oral bicarbonate 2%** is used to form a less soluble complex.
3. **Parenteral deferoxamine** Is indicated when serum iron level exceeds 350 mcg/dl. The dose is **10 mg/kg/hour ... I.V.** for up to 24 hours,
   or **90 mg/kg/dose ... I.M.** every 8 hours for 3 doses.

* Available preparation of deferoxamine is:

RI Desferal vial (500 mg).

(Practical dosage: The vial is diluted in 100 ml saline and infusion is made at a rate of 2 ml/kg/hour).

5. Cancer Chemotherapy

Class and generic name	Trade name (form and concentration)
A) Antimetabolites	
• Methotrexate:	*RI Methotrexate vials (5, 50 and 500 mg).* *RI Methotrexate tablets (2.5 mg).*
• Mercaptopurine:	*RI Leupurin tablets (50 mg).*
• Cytarabine:	*RI Cytarabine vial (100 mg/5 ml), (500 mg/5 ml).*
• Fluorouracil:	*RI Fluoro-Uracil vial. (250 mg/5 ml), (500 mg/5 ml).*
B) Alkylating agents	
• Cyclophosphamide:	*RI Endoxan vial (100 mg, 200 mg and 1000 mg).* *RI Endoxan tablets (50 mg).*
• Ifosfamide:	*RI Holoxan vial (1 gm and 2 grams).*
• Chlorambucil:	*RI Leukeran tablets (2 mg and 5 mg).*
• Busulfan:	*RI Myleran tablets (2 mg).*
• Thio TEPA:	*RI Thiotepa vial (15 mg).*
C) Antitumor antibiotics	
• Daunorubicin:	*RI Daunamycin vial (20 mg).*
• Doxorubicin:	*RI Adriamycin vial (10 mg and 50 mg).*
• Actinomycin D:	*RI Cosmegin vial (0.5 mg).*
• Bleomycin:	*RI Bleocin vial (15 mg).*
D) Vinca alkaloids	
• Vincristine:	*RI Vincristine vial (1 mg, 2 mg and 5 mg).*
• Vinblastine:	*RI Veblastin OR Cytoblastin vial (10 mg).*
• Vinorelbine:	*RI Navelbine vial (10 mg).*
F) Other drugs	
• Procarbazine:	*RI Natulan capsules (50 mg).*
• Dacarbazine:	*RI DTIC vial (100 mg and 200 mg).*
• Cisplatin:	*RI Platinol OR Cisplatin vial (10 mg).*
• Carboplatin:	*RI Paraplatin vial (50 mg and 150 mg).*
• Etoposide	*RI Vepesid amp. (100 mg) and capsules (50 mg).*
• Lomustine:	*RI CCNU capsules (40 mg and 100 mg).*
• Asparaginase:	*RI Crasnitin vial (2000 I.U and 10.000 I.U).*

Mechanism of action

Cancer chemotherapy depends on the idea that tumour cell division (cell cycling) is more rapid than that of normal cells. However, this fact is not absolutely true as bone marrow, mucosal surfaces of gut, hair follicles, reticuloendotheial system and germ cells are all dividing more rapidly than many cancer cells. This fact explains the occurrence of adverse effects on these tissues during chemotherapy.

All dividing (cycling) cells go through a series of phases: synthesis of DNA, synthesis of RNA, mitosis and rest. Generally, drugs are more active against actively cycling cells and least active against resting cells.

Drugs that kill cancer cells **(anticancer drugs)** may be:

(a) Cycle nonspecific: kill active and resting cells.
(b) Cycle specific: kill only actively cycling cells.
(c) Phase specific: kill only cells that are in a particular phase of active cycle.

- **Antimetabolites** inhibit the synthesis of folic acid, purine and pyrimidine.
- **Alkylating agents** cause alkylation of DNA and RNA.
- **Antitumor antibiotics** produce a complex with DNA.
- **Vinca alkaloids** produce a metaphase block (phase specific).
- **Etoposide** produces a delay in premitotic cell cycling (phase specific).
- **Actinomycin** and **procarbazine** inhibit DNA and RNA synthesis.

Principles of therapy

Cancer chemotherapy is usually combined, intermittent and prolonged.

- **Combined:** Several drugs are used simultaneously to have different sites of action and to attack cells at different phases of cycling. The chosen drugs depend on the nature and stage of the malignant tumour.
- **Intermittent:** After the initial maximal cell killing by drugs, an interval must be left for sufficient recovery of normal cells especially bone marrow, gut and immunologic system. An interval of 2 -3 weeks is usually sufficient.
- **Prolonged:** Several courses of drug therapy are usually needed to assure the complete eradication of malignant cells. A single leukemic cell, for example, is capable for multiplying and killing the patient.

Cancer chemotherapy should be only made in specialized centers and with physicians experienced in pediatric oncology. The role of the pediatrician is essentially the early diagnosis of malignant neoplasms and the rapid referral to specialized centers.

Cancer chemotherapy is usually combined with other lines of therapy as ***surgery, irradiation or bone marrow transplantation.***

Chemotherapy of common malignancies

1. Acute lymphoblastic leukemia

Treatment program includes 3 basic components:

a) Remission induction

A combination of prednisone, vincristine and asparaginase is usually sufficient to induce remission in most cases within 4 - 6 weeks. Remission is achieved when the bone marrow becomes free of any leukemic cells.

- Prednisone: 40mg/m^2/day … oral.
- Vincristine: 1.5 mg/m^2/dose … I.V … every week.
- Asparaginase: 6000 IU/m^2/day … I.M ... twice weekly.

b) CNS therapy

It starts with the onset of therapy, and continues for one year. It is made by intrathecal injection of 3 drugs:

- Methotrexate: 15 mg/m^2/dose.
- Hydrocortisone: 15 mg/m^2/dose.
- Cytarabine: 30 mg/m^2/dose.

Treatment is given every week for the first 6 weeks (during induction), then every 8 weeks for the first year.

c) Maintenance phase (systemic continuation treatment)

It starts after remission induction and continues for 2.5 - 3 years.
It is made by another 2 drugs:

- Mercaptopurine: 50 mg/m^2/day … oral.
- Methotrexate: 20 mg/m2/dose ... oral ... every week.

In case of relapse, after continuation, intensive course of cytarabine combined with other drugs may be effective.

2. Acute myelogenous leukemia

Treatment program includes also the 3 basic components:

a) Remission induction

A combination of cystosine arabinoside and duanorubicin will induce remission in 70% of cases in one week.

- Cytosine arabinoside: 100 mg/m^2 /dose ... continuous I.V infusion for 7 days.
- Daunorubicin: 30 mg/m^2/day ... I.V … for 3 days.

b) CNS therapy

Similar to that of acute lymphocytic leukemia.

c) Maintenance phase (systemic continuation treatment)

It is made by rotating combinations of several agents for about 2 years.

3. Hodgkin lymphoma

For early cases (stage I or IIA), radiation alone is the treatment of choice. In case of recurrence or in more advanced disease, a combination chemotherapy is required for about 6 months. There are 2 alternative regimens, each consists of 6 cycles of 4 drugs:

a) **MOPP regimen:** A combination of nitrogen **m**ustard, vincristine (**o**ncovin), **p**rocarbazine and **p**rednisone.

b) **ABVD regimen:** A combination of doxorubicin (**a**driamycin), **b**leomycin, **v**inblastine and **d**acarbazine.

4. Non-Hodgkin lymphoma (NHL)

For NHL, multiagent chemotherapy is the primary treatment.

a) **In early-stage NHL (stage I or II):** 6 cycles **COMP** (**c**yclophasphamide, vincristine (**O**ncovin), **m**ethotrexate and **p**rednisone) or 3 cycles of **COPA** (**c**yclophasphamide, vincristine (**O**ncovin), **p**rednisone and doxorubicin or **a**driamycin) can be used. This is followed by 6 months of mercaptopurine and methotrexate. About 90% of cases are cured with this regimen.

b) **In advanced-stage NHL (stage III or IV):** Therapy should be based on the histologis subtype.

5. Neuroblastoma

a) **For localized tumour,** surgical resection is the treatment of choice.

b) **In disseminated disease** (70% of cases), both irradiation and chemotherapy are required. A combination of cyclophosphamide and doxorubicin will induce remission in 50% of cases.

6. Wilms tumour

Immediate surgical removal of the kidney containing the tumour is the initial step of therapy. Postoperative combination chemotherapy is usually required for 6 months. For localized disease, actinomycin and vincristine are used together and for advanced disease, a third drug (doxorubicin) is needed.

6. Topical Medications

Protective and soothing applications
- Zinc oxide.
- Vaseline-Boric acid.
- Calamine.

Antimicrobial applications
- Antibacterial (Antibiotics).
- Antifungal.
- Antiparasitic.

Topical corticosteroids
- Nonflourinated preparations.
- Flourinated preparations.
- Steroids and antimicrobial combinations.

Keratolytic agents
- Salicylic acid and steroid preparations.
- Coal tar and steroid preparations.
- Salicylic acid, coal tar and steroid preparations.

Surface anesthetics
- Lignocaine and Cinchocaine.

Burns preparations
- Silver sulphadiazine.

Oral analgesics

Ear analgesics and ear wax softeners

Topical antihistamines are potent sensitizers and should never be used in practice.

A) Protective and soothing applications

• **Zinc oxide:** It is a useful protective agent, which is commonly used in newborns and young infants to prevent napkin dermatitis. A thin layer of the ointment or cream is applied to the napkin area, following each urination or defecation. It prevents contact of the skin with the irritant urine and stool.

* Available preparations are:

RI Zinc oxide ointment 10%.
RI Zinc olive lotion OR Zincolive lotion.
RI NO Rash cream OR A1 cream.
RI Baby cream OR Zincosil cream

• **Vaseline and boric acid:** It can be used as an alternative to zinc oxide for prevention of napkin dermatitis in newborns and young infants.

* Available preparation is:

RI Vaseline boric acid ointment.

- **Calamine:** It is a useful soothing and antipruritic agent. It is indicated in itchy lesions as chickenpox and papular urticaria. It can be used several times per day. The main disadvantage is its tendency to cake on the skin.

* It is available as lotions and creams:

Rl Calamine lotion.
Rl Calamyl OR Caladryl lotion.
Rl Calazol lotion.
Rl Calamidine lotion (contains calamine and zinc oxide).

B) Antimicrobial applications

1. Topical antibiotics: The efficacy of topical antibiotics in treatment of pyoderma is doubtful. Systemic antibiotic therapy is more effective in lesions as impetigo and ecthyma. When these preparations are indicated, the commonly used antibiotics should be avoided because of the risk of sensitization. Gentamicin, chloramphenicol and polymyxin B, are the mainly used drugs. Above 8 years, tetracyclines can be also used. Fusidic acid (sodium fusidate) is an effective antistaphylococcal agent. Ointments are the preferable form.

* Available preparations are:

- **Gentamicin:** ***RlGaramycin OR Cidomycin OR Farcocin topical ointment.***
- **Chloramphenicol:** ***Rl Verracetin OR Adcocetine topical ointment.***
- **Tetracycline and polymyxin:** ***Rl Terramycin topical ointment.***
  Rl Oxytetrine topical ointment.
- **Sodium fusidate:** ***Rl Fucidin OR Fusiderm OR Fusi ointment.***

2. Topical antifungal agents: Several drugs are available for treatment of cutaneous fungal infections. Monilial napkin dermatitis is the commonest fungal infection in newborns and young infants. As the lesions are commonly wet, creams are the preferable forms. 2 - 3 daily applications are sufficient.

* Available preparations are:

- **Nystatin:** ***Rl Mycostan cream.***
  Rl Mycostatin baby cream.
- **Miconazole:** ***Rl Daktarin cream.***
  Rl Miconaz cream.
- **Natamycin:** ***Rl Pimafucin cream.***
- **Clotrimazole:** ***Rl Canesten cream.***
  Rl Candistan cream.
  Rl Baycuten cream.

(Antifungal agents are also prescribed to mothers with monilial sore nipple)

3. Topical antiparasitic agents: Scabies and pediculosis are the most common cutaneous parasites in pediatric practice. The three main drugs are benzyl benzoate, gamma benzene hexachloride and malathion.

• **Benzyl benzoate** is useful for both scabies and pediculosis. It is available in 2 forms, lotion and cream:

Rl Benzanil lotion 25%

Rl Benzanil OR Benzyl bezoate OR Farco benzyl cream .

* ***For scabies:*** After a hot bath and rubbing of the whole body with soft brush and soap, the body is dried and the benzyl benzoate lotion or cream is applied over the whole body from the neck down. Special attention should be given to axillae, and skin folds. The head and neck should be avoided. A second application, from the neck downwards is made in the 2nd night. On the third night, the patient should bath and wear freshly ironed clothes. The old clothes and bed linen should be thoroughly washed and ironed to kill any remaining mites.

* ***For head lice:*** 10 ml of the lotion is rubbed into the hair and left overnight before combing out the dead nits in the morning, then the hair is washed. The cream can be used instead.

• **Gamma benzene hexachloride 1 %** is also useful for both scabies and pediculosis. It is available in 3 forms:

Rl Scabine lotion 1% OR Scabine cream 1%

* ***For scabies:*** The lotion or cream is used in a similar way to benzyl benzoate.

* ***For head lice:*** One application of the lotion at night is sufficient.

• **Both drugs** (Benzyl benzoate + Gamma benzene hexachloride) are available in one preparation: ***Rl Gammabenzyl lotion.***

• **Malathion 0.5%** is equally effective and can be used in a way similar to that of the above two drugs. It is only available in a lotion form:

Rl Prioderm OR Quick 30 lotion.

• **Other preparations:** Other preparations as Diethylene glycol ether (Licid) and D-Phenothin (No-Lice) or crotamiton (Eurax) can be also used.

Rl Licid lotion OR No-Lice lotion.

Rl Eurax lotion and cream.

C) Topical corticosteroids

- Topical corticosteroids are potent anti-inflammatory and antipruritic agents. The main indications for use in pediatric practice are: Severe napkin dermatitis, infantile eczema, seborrheic dermatitis and severe itching associated with acute or chronic allergic conditions.

- Topical corticosteroids are contraindicated in the following conditions: Viral infection of the skin as chickenpox and herpes simplex, tuberculous or syphilitic skin lesions and cutaneous reactions to vaccination.

- Topical corticosteroids are available in several forms. **Creams** are suitable for acute wet lesions, while **ointments** are suitable for chronic dry lesions. For napkin dermatitis, which is mainly wet, creams are the only suitable forms.

In general, the application of a thin layer, 2 times daily is sufficient. Duration of therapy should be as short as possible. For acute conditions, 3-5 days treatment is generally sufficient. For prolonged use in chronic conditions, the weak forms (nonflourinated) are preferable to minimize the complications.

Side effects of prolonged use are both local and systemic. Skin atrophy, hypopigmentation and telangiectasia may occur. Significant systemic absorption may occur with fluorinated forms and leads to temporary suprarenal suppression.

1. Nonflourinated preparations: These forms are suitable for mild to moderate cases and should be the first choice in pediatrics, because the side effects are minimal. Available drugs and preparations are:

- **Prednicarbate:** *RI Dermatop cream. and Dermatop ointment.*
- **Alcometazone:** *RI Perderm cream and Perderm ointment.*
- **Hudrocortisone:** *RI Hydrocortisone cream and Hydrocortisone ointment.*

2. Flourinated preparations: These powerful forms should be used cautiously and for short periods because of the high incidence of side effects. Available drugs and preparations (in increasing order of potency) are:

- **Flumethasone:** *RI Locacorten cream and Locacorten ointment.*
- **Triamcinolone:** *RI Kenacort cream and Kenacort ointment.*
- **Betamethasone:** *RI Betnovate cream and Betnovate ointment..*
- **Betamethasone valerate:** *RI Betaderm cream and Betaderm ointment..*
- **Betamethasone dipropionate:** *RI Diprosone cream and Diprosone ointment..*
- **Mometasone:** *RI Elecon cream and Elecon ointment.*
- **Diflucortolone:** *RI Nericide cream and Nericide ointment.*
- **Halomethasone:** *RI Sicorten cream and Sicorten ointment.*
- **Clobetasol propionate:** *RI Dermovate cream and Dermovate ointment..*
- **Fluticasone propionate:** *RI Cutivate cream and Cutivate ointment..*

3. Steroids and antimicrobial combinations: Topical steroids and anti-microbial preparations are useful in infected allergic conditions. Napkin dermatitis, superimposed with monilial infection is the commonest indication. Creams are the preferable forms. Available combinations are:

- **Hydrocortisone + miconazole:** *RI Daktacort cream.*
- **Betamethasone + miconazole:** *RI Micosone cream.*
- **Triamcinolone + econazole:** *RI Pevisone cream.*
- **Betamethasone + clotrimazole:** *RI Triderm OR Lotriderm cream.*
- **Halomethasone + triclosan:** *RI Sicorten-plus cream.*
- **Beclomethasone + miconazole + neomycin:** *RI Polyderm cream.*
- **Betamethasone + miconazole + fusidic acid:** *RI Fucisone-M cream.*
- **Triamcinolone + Nystatin + gramicidin + neomycin:**
  RI Kenacomb OR Amocomb OR Pandermal cream.
- **Betamethasone + clioquinol + gentamicin + chlorocresol:**
  RI Quadriderm cream.

D) Keratolytic agents

Keratolytic agents are useful in skin conditions associated with hyper-keratinization as seborrheic dermatitis, neurodermatitis, ichthyosis and psoriasis.

1. Salicylic acid and steroid preparations: They are particularly useful in treatment of cradle cap of the scalp and other forms of seborrheic dermatitis. One application per day for 3 - 4 days is usually sufficient.

* Available preparations are:

- **Salicylic acid + Flumethasone:** *RI Locasalen ointment.*
- **Salicylic acid +Triamcinolone:** *RI Cinolone S ointment.*
- **Salicylic acid + Betamethasone:** *RI Diprosalic ointment.*
- **Salicylic acid + Dexamethasone:** *RI Saligesic ointment.*

2. Coal tar, salicylic acid and steroid preparations: Useful in chronic keratinizing conditions especially psoriasis and ichthyosis.

* Available preparations are:

RI Dermotar ointment.
RI Cortar ointment.

E) Surface anesthetics

These preparations are indicated in severely painful conditions as:

- Severely painful sore nipple of lactating mother, where it can be applied to the sore nipple 10 - 15 minutes before suckling.
- Severe acute constipation, where the ointment can be applied to the anal area to minimize pain during defecation.
- Severe ulcerative stomatitis where local application 15 minutes before feeding is helpful.

* Available preparations are:

- **Cinchocaine:** *RI Neocaine cream.*
- **Lignocaine (Lidocaine):** *RI Lignocaine cream.*
  RI Lignocaine gel.
  RI Xylocaine cream.
  RI Xylocaine gel.
  RI Lidocaine gel.
  RI Ultracaine gel.
  RI Gelicaine gel.
  RI Lignopanthen gel.
  RI Farcocaine ointment.
  RI Lidosine ointment.

F) Burns preparations

Most preparations contain silver sulphadiazine and some preparations contain panthenol as well.

* Available preparations are:

RI Dermazin cream.
RI Silvazine cream.
RI Argiderm P cream.

G) Oral analgesics

These preparations are mainly used in ulcerative stomatitis to reduce the pain and to help oral feeding. They can be applied several times/day, preferably 10-15 minutes before feeding. They can be also used in difficult teething. Several forms of preparations are available including gel, paint, paste, spray, solution and lozenges.

* Available preparations are:

RI Dentinox teething gel OR Dento-gel teething gel.
RI Oracure gel OR Medijel gel OR Mundisal gel.
RI Dentocalm paint
RI Solcoseryl dental paste.
RI Orabase protective paste.
RI BBC spray.
RI Orofar solution.
RI Orofar lozenges.
RI Bradoral tablets.

H) Ear analgesics

Analgesic eardrops are mainly used in otitis media especially during the first day of illness. The dose is 1-2 drops, 3-4 times per day.

* Available preparations are:

RI Otocalm OR Otosept ear drops.
RI Otal ear drops.
RI Audax ear drops.
RI Ciloprine ear drops.

I) Ear wax softeners

Several preparations are available to soften hard ear wax. The softening material is usually carbamide peroxide in glycerin.

* Available preparations are:

RI Remowax ear drops.
RI Ear Wax ear drops.
RI Perroxy ear drops.

7. Eye Medications

Pediatricians should be able to manage simple ophthalmological conditions as mucopurulent conjunctivitis and allergic conjunctivitis. On the other hand, they should also be alert to detect cases of squint and errors of refraction and refer them to ophthalmological consultations. Eye medications of interest to pediatricians are:

A) Antibiotics.

B) Decongestants and antihistamines.

C) Corticosteroid eye preparations are serious drugs and should be mainly used by an ophthalmologist. The indiscriminate use of these drugs is a significant cause of blindness.

A) Antibiotics

Antibiotic eye drops or ointments are commonly used in pediatric practice for treatment of mucopurulent conjunctivitis. They are also used in the newborn, during the first 4 - 5 days, as a prophylactic measure against conjunctivitis.

Several antibacterial drugs are available. Chloramphenicol may be the drug of choice because of its broad-spectrum coverage and rare development of sensitization, but it is better to be avoided in the newborn because systemic absorption may lead to Grey syndrome. Other antibacterial drugs as polymyxin, neomycin, gramicidin, tetracyclines or aminoglycosides can be also used.

Before instilling eye drops or ointment, the eye should be washed with **boric acid lotion 2%** or normal saline.

The usual dosage is **1-2 drops, 3 - 4 times daily.** In severe infections, eye drops may be used up to 10 times/day (every 2 hours) and an oral antibiotic therapy should be also used. Eye ointment may be applied before sleep for a prolonged effect during night. Duration of therapy is usually 3 - 6 days.

* Available preparations are:

- **Chloramphenicol**

  RI Iso-Miphenicol OR Isopto-Fenicol eye drops.
  RI Ocuphenicol OR Optocetine eye drops.
  RI Miphenicol OR Epiphenicol eye ointment 1%.

- **Polymyxin + Neomycin ± Gramicidin or Bacitracin**

  RI Polyspectran OR Cebemyxine eye drops.
  RI Neo Pol OR Isopto-Statrol eye drops.
  RI Polyspectran OR Cebemyxine eye ointment.
  RI Neo-Bactin OR Neo-Polybactin eye ointment.

- **Gentamicin**
  RI Optigent OR Ophtagram eye drops.
  RI Garamycin OR Gentamicin eye ointment.
- **Tobramycin**
  RI Tobrex OR Tobrin OR Tobral OR Tobralex eye drops.
  RI Tobrex OR Tobrin eye ointment.
- **Oxytetracycline + Polymyxin**
  RI Terramycin OR Oxymycin OR Tetra eye ointment.

B) Decongestants and antihistamines

Decongestant eye drops are used for simple cases of allergic conjunctivitis. The usual dosage is **1 - 2 drops, 3 - 4 times daily.** An oral antihistamine is usually needed in severe cases. Available preparations are:

- **Naphazoline + chlorpheniramine**
  RI Prisoline OR Optozoline OR Neozoline eye drops.
  RI Prisoline zinc OR Nostamine eye drops.
- **Tetrahydrozoline**
  RI Visine OR Occuzoline eye drops.
- **Phenylephrine**
  RI Isopto-Frin OR Prefrin OR Phenylephrine eye derops.

C) Corticosteroid eye preparations

These preparations are used in severe allergic conditions not responding to simple decongestants. The usual dosage is 1 - 2 drops, 3 - 4 times daily. They should not be used for more than few days without ophalmological consultation.

- **Prednisolone:** *RI Isopto-sterofrin eye drops.*
- **Dexamethazone:** *RI Dexonium OR Isopto-Maxidex eye drops .*

.* Some preparations contain an antibiotic as well:

- **Gentamicin+ Prednisolone:** *RI Apigent-P eye drops and ointment.*
- **Gentamicin+ Dexamethazone:** *RI Dexamytrex eye drops and ointment.*
- **Tobramycin+ Dexamethazone:** *RI Tobradex eye drops and ointment.*
- **Neomycin+ Polymyxin B+ Dexamethazone:**
  RI Isopto -Maxitrol eye drops.
  RI Dexaron eye drops and ointment.
  RI Dexatrol eye drops and ointment.
  RI Maxitrol eye ointment.

8

Immunological Products

1. Active Immunization.
2. Passive Immunization.

1. Active Immunization (Vaccination)

Compulsory vaccination	
BCG vaccine:	0.1 ml ... intradermal.
Oral poliomyelitis vaccine:	2 drops ... oral ... 3 doses.
DPT vaccine:	0.5 ml ... I.M. ... 3 doses.
Hepatitis B vaccine:	0.5 ml ... I.M. ... 3 doses.
Measles vaccine:	0.5 ml ... subcutaneous.
MMR vaccine:	0.5 ml ... subcutaneous.
Other vaccines	
Meningococcal vaccine:	0.5 ml ... subcutaneous.
DT vaccine:	0.5 ml ... I.M.
Hemophilus influenza type b:	0.5 ml ... I.M. ... or subcutaneous, 1-3 doses.
Influenza vaccine:	0.5 ml ... I.M. ... or subcutaneous.
Hepatitis A vaccine:	0.5 ml ... I.M. ... 2-3 doses.
Chickenpox vaccine	0.5 ml ... I.M. ... or subcutaneous.
Rabies vaccine:	1.0 ml ... I.M. ... 5 doses (days: 0,3,7,14,28).

A) Compulsory vaccination

Time	Vaccine	Dose
At birth or during 1st month	— **BCG.**	— **0.1 ml (intradermal) in the left deltoid region.**
At the age of 2 months	— **Oral poliomyelitis.** — **DPT vaccine.** — **Hepatitis B vaccine.**	— **2 drops (oral).** — **0.5 ml (intramuscular).** — **0.5 ml (intramuscular).**
At the age of 4 months	— **Oral poliomyelitis.** — **DPT vaccine.** — **Hepatitis B vaccine.**	— **2 drops (oral).** — **0.5 ml (intramuscular).** — **0.5 ml (intramuscular).**
At the age of 6 months	— **Oral poliomyelitis.** — **DPT vaccine.** — **Hepatitis B vaccine.**	— **2 drops (oral).** — **0.5 ml (intramuscular).** — **0.5 ml (intramuscular).**
9 - 10 months	— **Measles vaccine.**	— **0.5 ml (subcutaneous).**
15 months	— **MMR vaccine.**	— **0.5 ml (subcutaneous).**
1 1/2 - 2 years	— **Oral poliomyelitis.** — **DPT vaccine.**	— **2 drops (oral).** — **0.5 ml (intramuscular).**
4 1/2 years	— **Oral poliomyelitis.** — **DPT vaccine.**	— **2 drops (oral).** — **0.5 ml (intramuscular).**

- **BCG vaccine**

It is a live attenuated tubercle bacilli vaccine, which gives considerable protection against tuberculosis and almost 100% effective in preventing tuberculous meningitis. It is given routinely to all newborns without prior tuberculin testing. When vaccination is delayed to the end of the first year, prior tuberculin testing is important. The vaccine can be also given to tuberculin negative children and adolescents.

The dose is **0.1 ml (intradermal) in the left deltoid region.**

Successful vaccination produces a small-indurated area (2 - 4 mm) after a period of 3 - 4 weeks. Side effects include local suppuration (which may persist for few weeks) and axillary lymphadenitis.

It is contraindicated in immunologically compromised patients and in patients with T-cell deficiency.

* Available preparation is:

RI B.C.G. vaccine (vial + 1 ml solvent = 10 doses).

- **Oral poliomyelitis vaccine**

It is a live attenuated vaccine of the 3 strains (trivalent vaccine), which gives a definite protection against poliomyelitis.

It is given in **3 doses, each of 2 drops (oral),** at the age of 2 months, 4 months and 6 months. A booster dose is given between the age of one and half and two years. A second booster dose may be given at the age of 4 1/2 years.

The vaccine is safe but it should be avoided during febrile illness or in patients with diarrhea. A period of fasting for 1-2 hours after vaccination is recommended.

* Available preparation is:

RI Poliomyelitis vaccine (vials of 10, 20 or 40 doses).

- **DPT vaccine**

It is a mixture of 3 vaccines (toxoids of diphtheria and tetanus and killed highly antigenic organisms of pertussis).

It is given to all infants with the same schedule of oral poliomyelitis vaccine. The dose is 0.5 ml intramuscular.

Side effects include local-reaction at the site of injection and fever that may start few hours after injection but rarely persists for more than 24 - 36 hours.

* Available preparations are:

RI DPT vaccine (vial of 10 ml = 20 doses).
RI DPT vaccine (vial of 0.5 ml = single dose).

- **Hepatitis B vaccine**

It is a recombinant DNA vaccine containing the purified surface antigen of the virus. It is produced by culture of genetically engineered yeast cells, which carry the relevant gene of the surface antigen of hepatitis B.

It is currently recommended to all infants at the age of 2, 4 and 6 months (same schedule of oral poliomyelitis and DPT vaccine). It is also indicated in children and adults who are at increased risk of infection especially health care personnel and patients subjected to repeated transfusions as patients in hemodialysis and oncology units and patients with thalassemia and hemophilia.

The dose in infants and children is **0.5 ml intramuscular.**

In adults, the dose is **1.0 ml intramuscular.**

* There are 3 different schedules of vaccination:

1. In young infants: 3 doses at the age of 2, 4 and 6 months.
2. Rapid course in those subjected to immediate risk of infection: 3 doses. The second and third doses are given after one month and two months of the first dose.
3. Slow course when the immediate risk is small: 3 doses. The second and third doses are given after one month and 6 months of the first dose.

Side effects include transient erythema and induration at the site of injection. Transient low-grade fever may also occur.

* Available preparations are:

RI Hepatitis B vaccine (1 ml/vial = 2 doses).
RI Hepatitis B vaccine (5 ml/vial = 10 doses).

• Measles vaccine

It is a live attenuated vaccine, which gives protection against measles. However, vaccinated children may contract measles, but the disease is usually milder and the picture is commonly atypical.

It is given to all infants at the age of 9 -10 months, but it can be also given to children and adolescents.

The dose is **0.5 ml subcutaneous (single dose).**

The vaccine is generally safe. Fever and coryza-like symptoms may occur 6 - 10 days after injection.

* Available preparations are:

RI Measles vaccine (vial + 0.5 ml solvent = single dose).
RI Measles vaccine (vial + 5 ml solvent = 10 doses).

• MMR vaccine

It is a mixture of 3 vaccines (live attenuated vaccines of measles, mumps and rubella). It is given to children at the age of 15 months. It can be also given to older children. A booster dose at the age of 6 years is currently recommended. The dose is **0.5 ml subcutaneous (single dose).** The vaccine is safe. Fever and coryza-like symptoms may occur 6 -10 days after injection.

* Available preparations are:

RI MMR vaccine (vial + 0.5 ml solvent = single dose).
RI MMR vaccine (vial + 5.0 ml solvent = 10 doses).

B) Other vaccines

- **DT vaccine**

It is a mixture of toxoids of diphtheria and tetanus. It is given to children above the age of 6 years. Pertussis vaccine is contraindicated after this age.

The dose is **0.5 ml intramuscular.**

* Available preparations are:

RI DT vaccine (vial of 10 ml = 20 doses)

RI DT vaccine (vial of 0.5 ml = single dose)

- **Meningococcal vaccine**

It is a live attenuated vaccine of meningococci group A and C. It is indicated during epidemics of meningococcal meningitis. It gives immunity for about 2 -3 years. The dose is **0.5 ml subcutaneous (single dose).** A booster dose may be given after 2 -3 years especially in school age children.

* Available preparation is:

RI Meningococcal vaccine (vial + 0.5 ml solvent = single dose).

- **Hemophilus influenza type b vaccine (Hib Vaccine)**

It is indicated for prevention of invasive bacterial diseases caused by hemophilus influenza type b especially meningitis, septicemia, cellulitis, arthritis and epiglottitis. It is particularly important in infants and young children below the age of 5 years where the incidence of infection with hemophilus influenza type b is most prominent.

The dose is **0.5 ml intramuscular or subcutaneous.**

The schedule of vaccination depends on the age at which vaccination starts:

1. In infants between 2-6 months of age, 3 doses are given at 2,3,4 months of age followed by a booster dose at the age of 18 months.
2. In infants between 6-12 months of age, 2 doses are given with one month apart followed by a booster dose at the age of 18 months.
3. In children between 1-5 years, single dose is sufficient without booster dosage. The site of injection in infants is the antero-lateral surface of the thigh (middle third) while in children it is in the deltoid region.

* Available preparation is:

RI ACT-Hib vaccine (vial + 0.5 ml solvent in syringe = single dose).

- **Influenza vaccine**

It is a vaccine active against the most common strains of influenza virus. It is indicated in children, above the age of one year, and adults who are at risk especially those with cardiac disease, metabolic disease and immunodeficiency. It is also recommended in asthmatic children with repeated episodes of respiratory infections.

The dose is **0.5 ml intramuscular or subcutaneous** for children above 6 years old and only **0.25 ml** for children between 1-6 years.

RI Fluarix vaccine (0.5 ml).

- **Hepatitis A vaccine**

It is a sterile suspension containing inactivated hepatitis A virus. It is indicated for active immunization against hepatitis A virus in subjects at risk of exposure especially in areas where the prevalence of hepatitis A is high (as in Asia, Africa, Mediterranean basin, Middle East, Central and South America). The vaccine can be given to adults and children above the age of one year.

The dose in children between 1-15 years of age is **0.5 ml, intramuscular.** In adults, the dose is **1.0 ml, intramuscular.** The schedule of vaccination consists of 2 doses. The second dose is given 6 months after the first.

RI Havrix vaccine 1440 (1.0 ml vial).

- **Chickenpox vaccine**

It is varicella virus live attenuated vaccine. It can be given to children above the age of one year in a dose of **0.5 ml, intramuscular or subcutaneous.** Above the age of 12 years, 2 doses are given with one month interval.

RI Varilrix vaccine (0.5 ml vial).

- **Rabies vaccine**

Vaccination against rabies is directed to unprovoked bite of a domestic or wild animal. Dogs and cats are the main offenders.

When the offending animal is under observation, vaccination can be withheld until the animal acts abnormally. On the other hand, if the biting animal ran away after an unprovoked bite, immediate vaccination is indicated. Local treatment of the puncture wound is equally important.

Recently, human diploid cell vaccine (HDCV) is available in **5 doses (1.0 ml intramuscular)** at 0, 3, 7, 14 and 28 days. Available preparation is:

RI Human Rabies vaccine (1.0 ml vial).

C) Recent combined vaccines

- **Combined vaccine DPT- HB**

This vaccine contains 4 vaccines together (triple vaccine of diphtheria, tetanus, pertussis in addition to hepatitis B vaccine). It is given to infants at 2, 4 and 6 months of age. Available preparation is ***Tritanrix HB (5 ml =10 doses).***

- **Combined vaccine DPT- Hib- Salk**

This is a pentavalent vaccine (DPT + Hemophilus influenza type b vaccine + Salk intramuscular vaccine of poliomyelitis). It is given to infants at the age of 2, 4 and 6 months. Available preparation is ***Pentact-Hib vaccine (0.5 ml vial).***

2. Passive Immunization

Antitoxins
Antitetanic serum: 50.000 - 100.000 unit (1/2 I.M. and 1/2 I.V.).
Antidiphtheretic serum: 60.000 - 120.000 unit ... slow I.V.

Human immunoglobulins
Intramuscular immunoglobulins (Gammaglobulins).
Intravenous immunoglobulins: 300 mg/kg/day ... I.V infusion ... for 4 - 5 days.

A) Antitoxins

Antitoxins are derived from the serum of hyper-immunized horses and are used for prophylaxis or treatment of diseases as tetanus and diphtheria.

Antitoxins are **serious drugs**. Severe allergic reactions and even fatal anaphylaxis may occur. Two important precautions are essential before the use of any antitoxin:
(a) A test dose of 0.2 ml of the serum is given subcutaneous. If no general reaction develops within 30 minutes, the rest of the dose can be given.
(b) Equipment for emergency intervention should always be available especially adrenaline, hydrocortisone, I.V. solution, endotracheal tube and oxygen.

• Antitetanic serum

- **For prophylaxis: 3000 - 5000 unit ... I.M.**
- **For treatment: 50.000 - 100.000 unit ... (1/2 I.M., 1/2 I.V.).**

Prophylaxis is only indicated in severely injured non-immunized persons. Treatment is indicated in patients with suspected or proved tetanus. 50.000 - 100.000 units are given as a single dose (half the amount I.M. and half I.V.).
* Available preparations are:

RI Tetanus antitoxin amp. (1500 unit/ml).
RI Tetanus antitoxin vial (30.000 unit/10 ml).

• Antidiphtheretic serum

- **For prophylaxis 10.000 unit ... I.M.**
- **For treatment: 60.000 - 120.000 unit ... slow I.V.**

Prophylaxis to non-immunized intimate contacts is generally not recommended. Treatment with antitoxin is indicated in patients with diphtheria.
* Available preparations are:

RI Diphtheria antitoxin amp. (4000 unit).
RI Diphtheria antitoxin vial (20.000 unit).

B) Human immunoglobulins

Human immunoglobulins are derived from the human plasma. They are useful for protection against several bacterial and viral infections. They are generally safe. Allergic reactions or anaphylaxis do not occur.

1. Intramuscular immunoglobulins (Gammaglobulins)

Nonspecific immunoglobulins (gammaglobulin) are derived from the pooled human plasma. The preparation contains antibodies, which protect passively against infections such as measles, chickenpox, hepatitis and poliomyelitis.
Gammaglobulins are indicated for:
(a) Prophylaxis against infection in persons at particular risk, e.g., an infant who is in contact to a case of chickenpox or measles.
(b) Treatment of patients with agammaglobulinemia.
The dose of **gammaglobulins** depends on the indication:

- For prophylaxis: **2 ml (320 mg) ... I.M.**
- For treatment of agammaglobulinemia:

- Loading dose: **1.4 ml/kg (224 mg/kg) ... I.M.**
  (The dose is given in divided doses over a week).
- Maintenance dose: **0.7 ml/kg (112 mg/kg) ... I.M ... every 4 weeks.**
  (The plasma level of immunoglobulins should be about 300 mg/dl).

* Available preparations are:

RI Gammaglobulin 16% amp. (320 mg/ 2 ml).
RI Globuman 16% vial (320 mg/2 ml).

2. Intravenous immunoglobulins

Intravenous immunoglobulins are particularly useful in immune disorders especially acute and chronic idiopathic thrombocytopenic purpura, severe cases of Guillain Barre syndrome and severe neonatal septicemia.

The dose is **300 mg/kg ... I.V. infusion (over 6 - 8 hours)**
... daily for 4-5 days.

Side effects may include transient fever, skin reactions, hypotension and shock.

* Available preparations are:

RI Sandoglobulin I. V. infusion, 1 gm (bottle of 33 ml = 30 mg/ml).
RI Sandoglobulin I. V. infusion, 3 gm (bottle of 100 ml = 30 mg/ml).
RI I.V.-Globulin infusion, 1 gm (vial + 20 ml solvent = 50 mg/ml).
RI I.V.-Globulin infusion, 2.5 gm (vial + 50 ml solvent = 50 mg/ml).
RI Vigam infusion, 2.5 gm (vial + 50 ml solvent = 50 mg/ml).
RI Vigam infusion, 5 gm (vial + 50 ml solvent = 100 mg/ml).

Practical dosage is 10 ml/kg (Sandoglobulin) or 6 ml/kg (I.V-Globulin or Vigam). Rate of infusion during the first hour should not exceed 1 ml/kg/hour.

9

I.V. Fluid Therapy

- **I.V. Solutions.**

1. **Shock Therapy.**
2. **Deficit Therapy.**
3. **Maintenance Therapy.**
4. **Therapy of Acid-Base and Electrolyte Disturbances.**
5. **Complications of I.V. Fluid Therapy.**

I.V Solutions

Main solutions
- Glucose 5%.
- Kadalex (glucose 5% + KCl).
- Normal saline 0.9%.
- Ringer's lactate.
- Neomaint solution (ready-made maintenance solution for neonates).
- Pediamaint solution (ready-made maintenance solution for children).

Other important additive solutions
- Potassium chloride 15%.
- Sodium chloride 3%.
- Sodium bicarbonate 5% and 8.4%.
- Calcium gluconate 10%.

A) Main solutions

These solutions are used to provide water, glucose and electrolytes.

Solution	Electrolyte content (mEq/liter)					Glucose (gm/liter)
	Na	Cl	K	Ca	lactate	
• Glucose 5 %	—	—	—	—	—	50
• Kadalex	—	27	27	—	—	50
• Normal saline 0.9%	154	154	—		—	—
• Ringer's Lactate	131	111	5	2	29	—
• Neomaint solution	30	40	10	—	—	120
• Pediamaint solution	37	57	20	—	—	100

B) Other solutions

These solutions are used to treat acid-base and electrolyte disturbances.

- **Potassium chloride 15%:** Each 1 ml contains 2 mEq of potassium. It is added to glucose: saline mixture to provide potassium.
- **Sodium chloride 3%:** Each 1 ml contains 0.5 mEq. of sodium. It is used in treatment of hyponatremia and hypernatremia.
- **Sodium bicarbonate 5% and 8.4%:** Each ml contains 0.6 mEq and 1mEq of bicarbonate respectively. It is used in treatment of metabolic acidosis.
- **Calcium gluconate 10%:** Each 1 ml contains 100 mg of calcium. It is used in treatment of hypocalcemia.

1. Shock Therapy

Shock therapy (over maximum 1 hour)
Ringer's lactate or normal saline: 20 ml/kg... I.V. infusion.
(May be given over 10 -15 minutes and may be repeated in severe cases).

Hypovolemic shock is a common complication of severe dehydration. Severe gastroenteritis in infants and diabetic ketoacidosis in children are the commonest causes. Clinical manifestations include tachycardia, hypotension and poor peripheral perfusion (cold extremities and skin mottling). In severe cases, altered consciousness becomes evident. Hypovolemic shock is corrected with ***volume expanders***, i.e. I.V. solutions that have the property of expanding the vascular volume by remaining intravascular.

- **Ringer's lactate: 20 ml/kg, I.V. over one hour.**

In severe cases, the calculated amount can be given over 10-15 minutes and can be repeated once or even twice.

It is the most suitable solution for initial therapy of hypovolemic shock. It should be immediately given in all types of dehydration even before serum electrolyte values are measured. Ringer's lactate solution has 2 main advantages:
(a) It remains intravascular because the concentration of electrolytes in the solution is almost similar to that of serum. This will correct the hypovolemia and improve the renal circulation.
(b) The lactate content is metabolized in the body to bicarbonate, which corrects the commonly associated metabolic acidosis.

When Ringer's lactate solution is not available, an equivalent solution can be prepared (700 ml saline + 250 ml glucose 5% + 50 ml sodium bicarbonate 5% + 2 ml potassium chloride 15%). This equivalent solution contains sodium (137 mEq/liter), chloride (112mEq/liter), potassium (4mEq/liter) and bicarbonate (30 mEq/liter). That solution has the advantage of containing bicarbonate, which is more physiologic than the lactate.

- **Normal saline 0.9%: 20 ml/kg, I.V... over 1 hour.**

It is the preferable volume expander in case of diabetic ketoacidosis. It can be also used when Ringer's lactate or equivalent solutions are not available.

- **Fresh blood or plasma transfusion: 10 ml/kg, I.V... over 1 hour.**

It may be used in severe cases of hypovolemic shock but only after initial correction with Ringer's lactate or normal saline.

In case of dehydration, ***shock therapy*** is immediately followed by ***deficit and maintenance therapies.***

2. Deficit Therapy

Deficit therapy (over 8 hours)

Amount given

Mild dehydration:	40 ml/kg (or maintenance x 0.4).
Moderate dehydration:	80 ml/kg (or maintenance x 0.8).
Severe dehydration:	120 ml/kg (or maintenance x 1.2).

Solutions used

Isonatremic dehydration:	Glucose 5% + saline mixture 1:1.
Hyponatremic dehydration:	Glucose 5% + saline mixture 1:1.
Hypernatremic dehydration:	Glucose 5% + saline mixture 4:1.

(KCl solution 15% is added in amount of 1 ml for each 100 ml solution).

Deficit I.V. fluid therapy is indicated in case of dehydration to replace the water and electrolyte losses. It should be carried out over 8 hours.

Expected losses of water and electrolytes

Solution used should provide the absolute losses of water and electrolytes:

(a) Water losses: it depends on the ***degree*** of dehydration (It is assessed by the severity of signs and the percentage of weight loss).

- Mild dehydration: 4% of body weight.
- Moderate dehydration: 8% of body weight.
- Severe dehydration: 12% of body weight.

(b) Electrolyte losses: It depends on the ***type*** of dehydration:

	Hyponatremic	Isonatremic	Hypernatremic
Sodium	**10-12 mEq/kg**	**8-10 mEq/kg**	**2- 4 mEq/kg**
Chloride	**10-12 mEq/kg**	**8-10 mEq/kg**	**2- 4 mEg/kg**
Potassium	**8 -10 mEq/kg**	**8-10 mEq/kg**	**2- 4 mEq/kg**

- **In isonatremic dehydration,** the ideal solution should contain: Sodium 80-100 mEq/liter, chloride 80-100 mEq/liter and potassium only 20 -30 mEq/liter. Complete correction of potassium deficit cannot be made in 24 hours, because the concentration of potassium in I.V. solution should not exceed 35- 40 mEq/liter.
- **In hyponatremic dehydration,** the concentration of electrolytes in the solution should be slightly higher.
- **In hypernatremic dehydration,** electrolyte losses are much less and the solution used should contain less electrolytes.

1. Solutions used in deficit therapy

(a) In isonatremic and hyponatremic dehydration, there are 2 choices:

1. Glucose 5% and normal saline in a ratio of 1:1 with addition of KCl 15% (1 ml for each 100 ml solution).

To make this solution, add
- Glucose 5%: 500 ml.
- Normal saline: 500 ml.
- KCl 15%: 10 ml.

The prepared solution will provide:
- Sodium: 77 mEq/liter.
- Chloride: 77 mEq/liter.
- Potassium: 20 mEq/liter.

2. Kadalex and normal saline in a ratio of 1:1. (500 ml of kadalex + 500 ml of normal saline).

The prepared solution will provide:
- Sodium: 77 mEq/liter.
- Chloride: 77 mEq/liter.
- Potassium: 13.5 mEq/liter.

This solution can be used when potassium chloride solution 15% is not available. It has the advantage of simplicity and disadvantage of lower potassium content.

(b) In hypernatremic dehydration, the solutions used for maintenance therapy are appropriate, i.e.:

1. **Glucose 5% and normal saline in a ratio of 4:1 with addition of KCl 15% (1 ml for each 100 ml solution).**
2. **Kadalex and normal saline in a ratio of 4:1.**

In case of suspected renal failure, deficit therapy should be given without adding potassium chloride solution until an adequate urine flow is obtained.

2. Calculation of the amount

The amount needed in deficit therapy depends on the degree of dehydration.
- In mild dehydration, it is about 40 ml/kg.
- In moderate dehydration, it is about 80 ml/kg.
- In severe dehydration, it is about 120 ml/kg.

Remarks

In patients with body weight above 10 kg, the amount is calculated as follow:
- In mild dehydration, it equals = maintenance x 0.4.
- In moderate dehydration, it equals = maintenance x 0.8.
- In severe dehydration, it equals = maintenance x 1.2.

In hypernatremic dehydration, give only 60% of the calculated amount, because full correction may result in cerebral oedema and convulsions.

3. Calculation of the rate of infusion

The calculated amount should be given in 8 hours. The rate of infusion depends on the method:

- **Standard drip method:** Where the rate is calculated as follow:
  - — Calculate the amount/hour: It equals the total amount divided by 8.
  - — Rate of infusion in drops/minute equals the amount/hour divided by 3 i.e. 45 ml/hour equals 15 drops/minute.
- **Micro-drip method:** Where a micro-dropper set (Solu-set) is used. In this method, the rate of infusion in micro-drops/minute equals the amount/hour i.e. 30 ml/hour ... equals 30 micro-drops/minute.
- **Infusion pump:** Where the rate of infusion in ml/hour can be easily and accurately adjusted.

Practical examples of deficit therapy

1. **A 6-kg infant with severe isonatremic dehydration. Order a deficit therapy.**
   - Solution used: Glucose 5% (500 ml) + Normal saline (500 ml) + KCl 15% (10ml).
   - The amount needed equals: 6 x 120 = 720 ml.
   - Rate of infusion (drops/minute) $= \dfrac{720}{8 \times 3} = 30$ drops/minute.

2. **A 9-kg infant with moderate hypernatremic dehydration. Order a deficit therapy.**
   - Solution used: Glucose 5% (800 ml) + Normal saline (200 ml) + KCl 15% (10 ml).
   - The amount needed equals: 9 x 80 = 720 ml. Give only 60% of the calculated amount i.e. 430 ml.
   - Rate of infusion (drops/minute) $= \dfrac{430}{8 \times 3} = 18$ drops/minute.

3. Maintenance Therapy

Maintenance therapy (over 24 hours)

Amount given

100 ml/kg/day ... for the first 10 kg body weight.

50 ml/kg/day ... added for each kg from 11-20 kg.

20 ml/kg/day ... added for each kg above 20 kg.

e.g. a child 17 kg needs (10 x 100) + (7 x 50) = 1350 ml/day.

Solutions used

Glucose 5% + saline mixture: 4:1.

(KCl solution 15% is added in amount of 1 ml for each 100 ml solution).

Maintenance I.V. fluid therapy is a common therapeutic procedure in pediatric practice. It is mainly used in the following conditions:

1. Following deficit therapy in dehydrated patients.
2. In critically sick patients as those with altered consciousness, severe respiratory distress or acute congestive heart failure. In these conditions, oral feeding may be hazardous as it may lead to serious aspiration.
3. Patients with severe persistent vomiting to prevent fasting dehydration.
4. Patients in the first few days of postoperative care where oral feeding is temporarily discontinued.

It is important to emphasize that maintenance I.V. fluid therapy should be used for the least possible time (2 - 3 days) and oral feeding should be resumed as soon as the condition permits. If oral feeding cannot be resumed after 2 - 3 days as in those with prolonged coma, or with continued severe distress, nasogastric tube feeding should replace I.V. fluid therapy (see tube feeding). If tube feeding is not tolerated (severe intestinal malabsorption) or contraindicated (following major abdominal surgery), maintenance I.V. fluid therapy should be replaced by total parenteral nutrition (see total parenteral nutrition).

Minimum daily requirements of water and electrolytes

The ideal I.V. maintenance solution should provide the minimum daily requirements of water and electrolytes.

(a) Water requirements: It depends on the ***body weight***:

- For 1 - 10 kg body weight: 100 ml/kg/day.
- For each kg from 11 - 20 kg, add 50 ml/kg/day.
- For each kg above 20 kg, add 20 ml/kg/day.

Examples

- A 7 kg infant needs 7 x 100 = 700 ml/day.
- A 15 kg child needs (10 x 100) + (5 x 50) = 1250 ml/day.
- A 24 kg child needs (10 x 100) + (10 x 50) + (4 x 20) = 1580 ml/day.

(b) Electrolyte requirements: Mainly sodium, chloride and potassium: Sodium (3mEq/kg/day), chloride (3 mEq/kg/day) and potassium (2mEq/kg/ day). The ideal solution for maintenance I.V. fluid therapy should contain: sodium (30 mEq/liter), chloride (30 mEq/liter) and potassium (20 mEq /liter).

1. Solutions used in maintenance therapy

The most suitable maintenance solution is made by one of 3 choices:

1. **Glucose 5% and normal saline in a ratio of 4:1 with addition of KCl 15% (1 ml/100 ml solution).**

To make this solution, add: Glucose 5 %: 800 ml.+ Normal saline: 200 ml + KCl 15 %: 10 ml.

The prepared solution will provide: Sodium (31mEq/liter), chloride (51 mEq/liter), potassium (20 mEq/liter). The high chloride content in this solution is due to the use of both saline (Na Cl) and KCl.

2. **Kadalex and normal saline in a ratio of 4:1.**

To make this solution, add: Kadalex: 800 ml. + Normal saline: 200 ml.

The prepared solution will provide: Sodium (31mEq/liter), chloride (52 mEq/liter) and potassium (21 mEq/liter).

3. **Ready-made maintenance solution (Pediamaint I.V. solution):** This solution provides: Sodium (37 mEq/liter), chloride (57 mEq/liter), potassium (20 mEq/liter). It has the advantage of providing glucose 10% instead of 5%.

Remarks

- Potassium should not be added to patients with suspected or proved acute renal failure except after adequate urine flow is obtained. When an extra-amount of potassium is required, the maximum concentration of potassium in the solution should not exceed 40 mEq/liter. Potassium chloride solution should never be injected directly I.V.
- Glucose 10% can be used instead of the 5% solution, when extra-calories are required as in CNS infections. In this case, Pediamaint solution can be used.
- Calcium is not essential during the first 24 hours, but should be used from the second day in a dose 1-2 ml/kg of calcium gluconate 10% given by slow I.V.

2. Calculation of the amount/day

The amount needed/day is equal to the water requirements ... i.e:

- 100 ml/kg/day ... for the first 10 kg body weight.
- 50 ml/kg/day ... added for each kg from 11-20 kg.
- 20 ml/kg/day ... added for each kg above 20 kg.

(a) In neonatal period and early infancy, the amount can be increased up to 150 ml/kg/day.

(b) The amount is increased in the following conditions:

1. Fever: Add 10% for each degree above 38.0 °C (rectal).

2. Phototherapy: Add 10%
3. Infants placed in radiant warmer: Add 20%
4. Continued losses as diarrhea: Add 30%

(c) The amount is decreased in the following conditions:

1. CNS infections or brain oedema: Subtract 30%
2. Heart failure: Subtract 30%.
3. Hypernatremic dehydration: subtract 30%.
4. Mechanical ventilation: Subtract 10%.
5. Severe oliguria or anuria: Give only the insensible water losses.

3. Calculation of the rate of infusion

The calculated amount is given over 24 hours. The rate of infusion depends on the used method (see deficit therapy).

Practical examples of I.V. maintenance therapy

1. A 7 kg infant with persistent vomiting and temperature 39°C (rectal). Order a maintenance fluid therapy.

- Solution used: glucose 5% (800 ml) + normal saline (200 ml) + KCl 15% (10 ml).
- The amount/day equals: 7 x 100 = 700 ml. Add 10 % (70 ml) for the one degree rise in body temperature, so total amount is 770 ml.
- Rate of infusion (drops/minute) = $\frac{770}{24 \times 3}$ = 10 drops/minute.

2. A 15-kg child with severe bacterial meningitis. Order a maintenance fluid therapy.

- Solution used: glucose 10% (800 ml) + normal saline (200 ml) + KCl 15% (10 ml).
- The amount/day equals: (10 x 100) + (5 x 50) = 1250 ml. Subtract 30% (375 ml) because with CNS infections, there is inappropriate secretion of antidiuretic hormone. So, the total amount is 875 ml.
- Rate of infusion (drops/minute) = $\frac{875}{24 \times 3}$ = 12 drops/minute.

3. A 10-kg infant with severe acute congestive heart failure. Order a maintenance fluid therapy.

- Solution used: glucose 5% (800 ml) + normal saline (200 ml) + KCl 15% (10 ml).
- The amount /day equals: 10 x 100 = 1000. Subtract 30% (300 ml), So, the total amount is 700 ml.
- Rate of infusion (drops/minute) = $\frac{700}{24 \times 3}$ = 9 drops/minute.

4. Therapy of Acid-Base and Electrolyte Disturbances

> **Metabolic acidosis**
> 4 ml/kg of sodium bicarbonate solution 5% ... slow I.V. or
> 2 ml/kg of sodium bicarbonate solution 8.4%.
> **Hyponatremia**
> 5 - 10 ml/kg of sodium chloride solution 3% ... slow I.V.
> **Hypernatremia**
> 5 - 10 ml/kg of sodium chloride solution 3% ... slow I.V.

Several acid-base and electrolyte disturbances are commonly encountered and necessitate modification of standard I.V. fluid therapy. These problems are:

1. Metabolic acidosis

Acute metabolic acidosis is the most common acid-base disturbance. Severe gastroenteritis and dehydration in infants and acute renal failure or diabetic ketoacidosis in children are the most important causes. Salicylate poisoning should be also considered. Occasionally, acute metabolic acidosis occurs in episodes in patients with renal tubular acidosis, aminoacidopathies or glycogen storage disease type I.

Severe metabolic acidosis is detected clinically by deep rapid respiration (acidotic breathing). This respiratory pattern is not caused by the acidosis itself but by the respiratory compensation to wash the CO_2 out.

Laboratory diagnosis is by blood gas analysis where pH, bicarbonate and $PaCO_2$ are all low. Accordingly, metabolic acidosis can be classified as:

- **Mild:** pH below 7.3 and bicarbonate below 16 mEq/liter.
- **Moderate:** pH below 7.2 and bicarbonate below 13 mEq/liter.
- **Severe:** pH below 7.1 and bicarbonate below 10 mEq/liter.
- **Profound:** pH below 7.0 and bicarbonate below 7 mEq/liter.

With severe or profound metabolic acidosis, altered consciousness occurs.

Treatment of metabolic acidosis with **sodium bicarbonate** is indicated in moderate, severe and profound cases. It is made by one of 2 methods:

(a) Empirical correction: It can be made when facilities for blood gas analysis are not available. The dose is **2 mEq/kg, I.V. over 10 minutes**. This dose is equivalent to: **4 ml/kg of sodium bicarbonate solution 5%.**
or 2 ml/kg of sodium bicarbonate solution 8.4%.

(Each 1 ml/kg of the 5% solution will raise the serum bicarbonate level by about 1 mEq, while each 1 ml/kg of the 8.4% solution will raise the serum bicarbonate level by about 2 mEq).

(b) Accurate correction: It depends on the serum bicarbonate level (by blood gas analysis). Venous sample is satisfactory. The dose of sodium bicarbonate in mEq/kg is calculated from the following formula:

$NaHCO_3$ (mEq/kg) = 0.5 (Desired bicarbonate — Actual bicarbonate)

Example

- Desired bicarbonate is 16 mEq/liter.
- Actual bicarbonate is 10 mEq/liter.

So, the dose of bicarbonate is 0.5 (16 - 10) = 0.5 x 6 = 3 mEq/kg.
This dose is equivalent to:

- 6 ml/kg of the 5% solution or
- 3 ml/kg of the 8.4% solution.

Remarks

1. Blood gas analysis should be repeated after 15 minutes. The sodium bicarbonate therapy can be repeated every 15 minutes until the pH becomes above 7.25 and bicarbonate above 15 mEq/liter. Failure of response to therapy should suggest persistent pathology especially severe anoxia or shock.
2. Full correction should be avoided because the compensatory mechanisms of the body usually play a part in the process of correction, and iatrogenic metabolic alkalosis may occur.
3. With repeated sodium bicarbonate therapy, measurement of serum sodium level is also important because iatrogenic hypernatremia may occur.
4. In dehydrated patients, therapy should be delayed until shock therapy with Ringer's lactate is completed, because correction of shock, improvement of renal circulation and the lactate content usually correct the acidosis. If acidosis persists after shock therapy, evaluation of renal function is important and correction with sodium bicarbonate is indicated.

Treatment of the cause of metabolic acidosis is equally important:

(a) Control of diarrhea in patients with severe gastroenteritis.
(b) Insulin therapy in diabetic ketoacidosis.
(c) Other aspects of management in patients with acute renal failure.
(d) Oxygen therapy or mechanical ventilation in acute respiratory failure.

2. Hyponatremia

Hyponatremia with serum sodium level below 120 mEq/liter is usually symptomatic (convulsions or shock). The aim of therapy is to raise serum sodium level to 125 mEq/liter.

Treatment is made with **sodium chloride 3% solution.** Each 1 ml/kg of this solution will raise the serum sodium level by about 1 mEq.

The dose in ml/kg = 125 - actual serum sodium level.

Example

If serum sodium level is 117 mEq/liter,

Then, the dose of sodium chloride solution = (125 - 117) = 8 ml/kg.

Remarks

1. I.V. infusion should be **slow with the rate of 1 ml/minute.**
2. The maximum dose/time is **10 ml/kg.** In patients with serum sodium level below 115 mEq/liter, treatment should be made in multiple doses with 2 hours interval between each 2 doses. Serum sodium level should be measured after each dose.

Another example

A child 1 year old (10 kg) with serum sodium 105 mEq/liter.

The required amount for correction = 10 (125 - 105) = 10 x 20 = 200 ml so, treatment will be made in 2 doses:
First dose = 100 ml (I.V. over 100 minutes).
Second dose (2 hours later) = 100 ml (I.V. over 100 minutes).

3. Hypernatremia

Hypernatremia (serum sodium level above 150 mEq/liter) is a potentially serious condition that may result in cerebral damage and widespread cerebral hemorrhage and thrombosis.

Clinically, convulsions and/or altered consciousness may be evident and permanent neurological sequelae may occur.

Hypernatremic dehydration is the commonest cause, but the condition may also occur iatrogenically by the use of concentrated milk formula or excessive administration of sodium bicarbonate.

Successful management of hypernatremic dehydration depends on 3 basic rules:

(a) Undercorrection: Give only 60% of the calculated deficit because full correction may result in cerebral edema and convulsions and give only 70% of the calculated maintenance because associated excessive secretion of antidiuretic hormone is usually present. As the solution used in deficit and maintenance therapy of hypernatremic dehydration is essentially the same, the simplest practical method of management is to **ignore the dehydration** and give the maintenance solution (130 ml/kg) over 24 hours.

(b) Slow correction: As convulsions frequently occur with rapid return of serum sodium to normal, slow correction is important to avoid convulsions. The maximum reduction rate of serum sodium level should not exceed 10 mEq/liter/day.

(c) Treatment of convulsions: Early recognition and treatment of possible associated convulsions is important to prevent cerebral damage.

Convulsions are mostly caused by *cerebral edema*. Treatment is made by the use of a **hypertonic solution**, which increases the osmolarity of the blood and draws fluids out of brain cells into the blood (cerebral dehydrating effect).

- Sodium chloride solution 3% (5 ml/kg, slow I.V.) or
- Mannitol 20% solution (10 ml/kg, I.V. over 30 minutes) can be used.

Convulsions may be also caused by *hypocalcemia*, so measurement of serum calcium level is also important. Hypocalcemia is treated by **calcium gluconate** 10% (1 ml/kg, I.V. over 10 minutes).

Convulsions not controlled by hypertonic solutions or calcium therapy necessitates **anticonvulsant drugs**. Diazepam is given I.V. in a dose of 0.5 mg/kg. If convulsions cease during injection, don't complete the calculated dose. Serious serum sodium level above 180-200 mEq/liter may necessitate peritoneal dialysis.

4. Hypokalemia

Acute severe hypokalemia with serum potassium level below 3 mEq/liter may result in muscle weakness, abdominal distension, paralytic ileus and renal tubular injury (inability to concentrate urine).

Treatment is made by increasing the concentration of potassium in the I.V. solution to **35 mEq/liter**. A maintenance solution containing this concentration is made as follows:

800 ml glucose 5% + 200 ml saline + 17.5 ml potassium chloride 15%

(Each 1 ml potassium chloride 15% provides 2 mEq of potassium).

Duration of therapy is guided by serum potassium level. Clinical manifestations of deficiency usually take several days to subside, and treatment can be continued with oral potassium (see mineral therapy).

5. Hyperkalemia

Acute renal failure is the main cause of hyperkalemia (see acute renal failure).

5. Complications of I.V. Fluid Therapy

Unfortunately, I.V. fluid therapy is an area of several **iatrogenic complications.** However, all these complications are preventable and can be avoided by the proper evaluation, proper calculation and careful administration. The most commonly encountered complications are:

1. Rapid infusion: I.V. fluids given at a rate higher than that calculated can lead to volume overload and acute congestive heart failure. In patients with hypernatremic dehydration, rapid infusion will often lead to cerebral oedema with altered consciousness and convulsions. Frequent inspection of the infusion rate is essential to avoid these complications.

2. Overinfusion: Improper calculation and excessive administration of I.V. fluids will lead to overhydration with puffiness of eyelids, hardening of the skin (acquired scleroderma) and generalized oedema. However, the condition my also occur with properly calculated amount if the patient is having acute renal failure or excessive secretion of antidiuretic hormone.

3. Electrolyte disturbances: Several complications may arise:

- **Hyponatremia:** Due to correction of isonatremic dehydration with a hypotonic solution as glucose 5% and saline mixture in a ratio of 4:1.
- **Hypernatremia:** Due to excessive use of sodium bicarbonate.
- **Hypokalemia:** Due to use of solutions with low potassium content.
- **Hyperkalemia:** Due to use of solutions containing potassium in patients with acute renal failure.

4. Infections: Bacteremia or septicemia may occur if strict aseptic techniques are not carefully followed. As a rule, the infusion bottles and the infusion set should be changed every day.

5. Nutritional deficiencies: Prolonged I.V. fluid therapy for more than 3 - 5 days will lead to nutritional deficiencies. If I.V. fluid therapy is necessary for more than a few days, nasogastric tube feeding or total parenteral nutrition should be considered.

6. Local complications at the I.V. site: The most frequent complications are extravasation (swelling at the infusion area) and pyogenic infections. Thrombophlebitis may also occur. Frequent inspection of the I.V. site (every hour) is essential for early detection of these complications. The I.V. cannula should not be left at one site for more than a few days.

10

Oxygen Therapy

- **Physiologic Considerations.**

1. **Indications.**
2. **Methods of Administration.**
3. **Dosage.**
4. **Duration of Therapy.**
5. **Complications.**

Oxygen Therapy

Oxygen is a drug. It has its own indications, methods of administration, dosage, duration of therapy and complications.

Physiologic considerations

Oxygen is the most essential element for life. Breathing in oxygen-free atmosphere is fatal in 4 minutes.

The normal concentration of oxygen in air is 21%. In other words, the **fraction of inspired oxygen (FIO2)** in air is 0.21. In case of breathing in pure oxygen atmosphere, the FIO_2 becomes 1.0. In case of oxygen therapy, dosage (or FIO_2) is ranging between 21 - 100% (or FIO_2 of 0.21 - 1.0).

The process of oxygenation is a process of "pressure difference". The oxygen moves from the high-pressure environment to that of low pressure. i.e., oxygen moves from the atmosphere to the alveoli, arterial blood and tissues because the pressure of oxygen in atmosphere is higher than that in the alveoli, arterial blood and tissues.

The **pressure of inspired oxygen (PIO2)** in air is calculated from the following equation:

$$PIO_2 = FIO_2\ (Bp - H_2Op)$$

- FIO_2: Fraction of inspired oxygen (0.21)
- Bp: Barometric pressure (760 mmHg)
- H_2Op: Water vapour pressure (48 mmHg)

$PIO_2 = 0.21\ (76 - 48) = 150$ mmHg

This is the pressure responsible for oxygenation, while breathing atmospheric oxygen ($FIO_2 = 0.21$) at sea level (Bp = 760 mmHg). With oxygen therapy, the pressure of inspired oxygen increases because of the increased FIO_2. At high altitude, the pressure decreases due to decreased barometric pressure.

The **pressure of alveolar oxygen (PAO2)** can be calculated from the following equation:

$$PAO_2 = PIO_2 - \frac{PaCO_2}{R}$$

- PIO_2: Pressure of inspired oxygen (150 mmHg)
- $PaCO_2$: Pressure of arterial CO_2 (40 mmHg)
- R: Factor equals 0.8

$$PAO_2 = 150 - \frac{40}{0.8} = 100 \text{ mmHg.}$$

This is the pressure of oxygen in alveoli, while breathing atmospheric air at sea level.

The **pressure of arterial oxygen (PaO_2)** is slightly lower than that of alveolar oxygen because of the normal physiological shunting. i.e. some of the alveoli are ventilated without being perfused.

In normal conditions, **PaO2 = 90 - 95 mmHg.**

Practical applications

The above mentioned oxygen equations are very important, as they demonstrate clearly the following important facts:

1. In **normal conditions**, any rise in FIO_2 is accompanied with equivalent rise in PIO_2 and PaO_2, e.g.:

- With air breathing ($FIO_2 = 0.21$), PaO_2 is 90 mmHg.
- With 40% O_2 breathing ($FIO_2 = 0.4$), PaO_2 becomes 180 mmHg.
- With 60% O_2 breathing ($FIO_2 = 0.6$), PaO_2 becomes 270 mmHg.
- With 100% O_2 breathing ($FIO_2 = 1.0$), PaO_2 becomes 450 mmHg.

2.In case of alveolar pathology, as severe pneumonia, there is a degree of **ventilation/perfusion mismatch,** so, the rise in PIO_2 is NOT accompanied with equivalent rise in PaO_2 e.g.: If PaO_2 is 50 mmHg at FIO_2 of 0.21, PaO_2 may become only 80 mmHg at FIO_2 of 0.6.

3.To assess the degree of ventilation-perfusion mismatch, several indices are made. These **"oxygen derived pulmonary indices"** can be used to evaluate the degree of intrapulmonary shunt as well as to compare different blood gas results in the same patient. The most commonly used indices are:

- **Arterial/alveolar oxygen ratio (PaO_2/PAO_2)**

  The normal ratio is 0.8 - 0.9. Value below 0.5 indicates severe pathology.

- **Arterial/inspired oxygen ratio (PaO_2/FIO_2)**

  The normal ratio is 400 - 450. Values below 200 indicate severe pathology.

1. Indications of oxygen therapy

1. The main indication of oxygen therapy is **arterial hypoxemia** (PaO_2 below 60 mmHg). Clinically, any patient with manifestations of respiratory distress (rapid respiration and retractions) is in need of oxygen. Cyanosis with respiratory distress is an urgent indication of oxygen therapy. Severe pneumonia, acute bronchiolitis, acute severe asthma and acute heart failure are the commonest indications.

2. Other indications of oxygen therapy are **neonatal apnea, shock** and **acute severe brain insult**. In comatose patient, oxygen therapy is important to preserve the vitality of brain cells (see management of comatose patient).

2. Methods of administration

* The system of oxygen administration is consisting of:

1. **Oxygen source:** Either oxygen cylinder or central piping system with wall outlets.
2. **Oxygen flowmeter:** To measure the flow of oxygen in liters/minute. e.g. 4 liters/minute, 7 liters/minute etc...
3. **Oxygen humidifier:** To humidify the dry oxygen. Some humidifiers are also capable for heating the oxygen "heating humidifiers".
4. **Oxygen enriched atmosphere:** It is the method by which the oxygen is administered.
5. **Oxygen analyzer:** To measure oxygen concentration in the oxygen enriched atmosphere especially with the head box.

* Oxygen can be given by several methods:

1. Inside an incubator: Each incubator is having an opening to provide oxygen. The oxygen concentration is related to the oxygen flow in liters/minute. With this method, it is very difficult to have an oxygen concentration above 40 - 50%. The main disadvantage of this method is the relatively low oxygen concentration. Moreover, it is only suitable for neonates and young infants.

2. Head box or Hood: It is a Plexiglas box with an opening to provide oxygen. It is placed over the head while the patient is lying in supine position. It is the method of choice for several reasons. It is suitable for all ages including neonates inside the incubators. The oxygen concentration inside can be increased up to almost 100%. The oxygen concentration is constant inside and does not change with repeated examination as in case of incubators and oxygen tents.

3. Oxygen masks: There are different types and sizes of oxygen masks suitable for all ages. Some of them (Venturi masks) can deliver precise oxygen concentrations (as 24%, 30%, 35%, 40%, 50%, 60%.). Oxygen masks should be made of clear vinyl for better comfort and visibility. The main disadvantage of masks is that infants and young children may not tolerate them. Moreover, the oxygen concentration cannot be accurately measured.

4. Nasal prongs: The oxygen flow requirement is usually 1-6 liters/ minute and this provides 24-50% oxygen concentration. With this method, the nasopharynx acts as a reservoir, providing an oxygen enriched atmosphere for both mouth and nose breathers. The main disadvantage is that the oxygen concentrations cannot be known or precisely measured.

5. Oxygen tent: It is rarely used as it has several disadvantages. The oxygen concentration inside cannot be increased for more than 40-50%. It makes observation difficult and the oxygen concentration decreases markedly with each examination.

6. Endotracheal tube: It is the method used in patients who are in need of continuous positive airway pressure (CPAP) or mechanical ventilation.

3. Dosage of oxygen

1.Oxygen should be given in a concentration that relieves cyanosis and corrects the arterial hypoxemia. Practically, start with 40% oxygen. The concentration can be then increased or decreased according to the clinical response and blood gas analysis. In case of cyanosis, start with 100% oxygen and decrease gradually (over few hours) to 40 – 60%.

2. Accurate dosage depends on the *measurement of arterial blood gases*. The proper dose is the oxygen concentration, which makes the arterial oxygen pressure (PaO_2) around 90 mmHg. *Measurement of arterial oxygen saturation (SaO_2)* can be made by the "pulse oximetry" which allows continuous noninvasive monitoring of oxygen saturation. The proper dose is the oxygen concentration that keeps arterial oxygen saturation above 90% (normal saturation is 95- 98%).

3. Once oxygen is indicated, it should be used *continuously*. Interrupted oxygen therapy is physiologically harmful especially to sick infants and young children.

4. *Persistent arterial hypoxemia* (PaO_2 below 50 mmHg) with 60% oxygen is an indication of endotracheal intubation and continuous positive airway pressure (CPAP) or mechanical ventilation. Arterial hypercarpia ($PaCO_2$ above 60 mmHg) is also an indication of mechanical ventilation.

4. Duration of oxygen therapy

1. Oxygen should be used for the *least possible time* needed to relieve the arterial hypoxemia. The actual duration depends mainly on the pathology. It may be only for few hours (as in acute severe allergic asthma) or it may extend for several days (as in severe pneumonia) or several weeks (as in bronchopulmonary dysplasia).

2. Oxygen should be *withdrawn gradually*. With oxygen concentrations above 40%, decrements of 10% per time are appropriate e.g. from 60% to 50% to 40%. With levels below 40%, decrements should be of 5% per time, e.g. 40%, 35%, 30%, 25% then discontinue. It is important to remember that abrupt oxygen withdrawal is very serious and it may precipitate a cardiopulmonary arrest.

5. Complications of oxygen therapy

Complications of oxygen therapy are related to both concentration (dosage) and duration of therapy. So, *"oxygen should be given with the lowest possible concentration and for the least possible time"*.

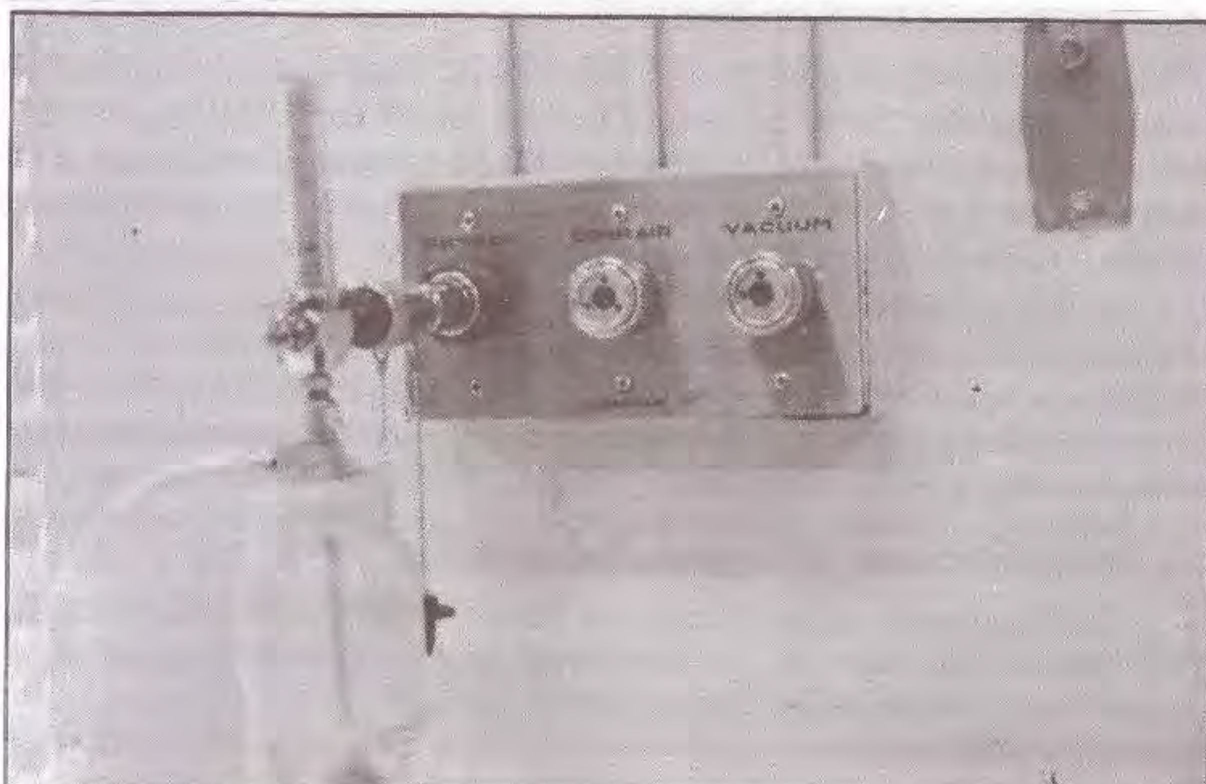
The main complications are:

1. Eye toxicity: Retrolental fibroplasia is a systemic oxygen toxicity, which occurs mainly in premature infants due to excessive PaO_2 delivered to the retinal artery. In these infants, arterial oxygen pressure (PaO_2) should never exceed 100 mm Hg and examination for retrolental fibroplasia should be made at the time of discharge and also 3 to 6 months later.

2. Lung toxicity: Pulmonary oxygen toxicity is related to concentration and duration of oxygen therapy. Breathing of 100% oxygen for 4 hours is toxic to the lungs, while 70% oxygen is toxic in 4 days. 40% oxygen is safe for one month. The lung toxicity is manifested by cessation of mucociliary activity, decreased production of surface-active material, atelectasis and ventilation-perfusion mismatch. Oxygen is particularly serious in mechanically ventilated prematures who may develop bronchopulmonary dysplasia with worsening of the pulmonary functions.

3. Oxygen dependency: With prolonged oxygen therapy, the patient becomes "oxygen dependent" and weaning becomes very difficult. In these cases, a very gradual withdrawal is important for successful weaning.

Oxygen source, flowmeter and humidifier



Oxygen therapy with a head box



Oxygen therapy with Venturi oxygen mask



Oxygen analyzer (to measure oxygen concentration)



Pulse oximeter (to measure arterial oxygen saturation)



Part Two

Practical Management

"I don't want two diseases,
one nature-made and one doctor-made"
Napoleon Bonaparte,
1820

How to Write a Prescription

The prescription is the image of the physician. It can clearly reflect his diagnostic abilities, therapeutic accuracy as well as his personality.

It is a shame for any physician to write a **"faulty prescription"** and it also may create several problems. It has been estimated that about 20% of therapeutic mistakes are caused by faulty prescriptions. Certainly, the ugly habit of writing prescriptions with bad handwriting and unclear letters is greatly responsible for many mistakes made by the pharmacists and the parents. Self-confident doctors always write clear prescriptions.

Correct prescription should fulfill the following criteria:

1. The physician: The name of the doctor, his qualifications, his clinic address and his telephone number should be included in any prescription.

2. The patient: The name of the child, his age (birth date), his weight and his temperature should be clearly included. The clinical diagnosis may be also mentioned.

3. Drug therapy: As a rule, use the least possible number of drugs. The trade name or the generic name of each drug should be written with clear and unmistakable handwriting. The concentration of the drug prescribed should be also included. The instructions should specify clearly the dose, the number and timing of doses per day and the duration of therapy. The abbreviation ***RI*** that is commonly written before each drug means **Recipe.** It is a historical habit that is not important in writing prescriptions.

4. Diet and activity: When treatment necessitates any specific change in diet or any restriction of activity, it should be clearly included.

5. Date of examination and date of suggested check-up: These dates are extremely important for proper follow up.

6. Signature of the physician.

Example

A child, 6 years old (20 kg) with tonsillitis (streptococcal pharyngitis).

RI Erythrocin OR Erythrin suspension (200 mg/5 ml)
One and half teaspoon (7.5 ml), oral, every 8 hours for 10 days.

RI Cetal OR Temporal syrup (250 mg/5ml)
One teaspoon (5 ml) when temperature exceeds 38°C, every 4 - 6 hours (when necessary).

When to Hospitalize

Hospital management is indicated for several pediatric problems. The main indications can be categorized in 3 groups:

1. Treatment of acute critical illness: Pediatric emergencies often involve every system:
- Acute respiratory conditions: Stridor, pneumonias and acute severe asthma. Cardiopulmonary arrest is an emergency of 4 minutes.
- Acute cardiac conditions: Myocarditis, endocarditis, pericarditis and acute congestive heart failure.
- Acute neurological conditions: Convulsions, coma and CNS infections.
- Acute renal conditions: Acute renal failure.
- Acute endocrinal conditions: Diabetic ketoacidosis.
- Metabolic conditions: Acute metabolic acidosis and tetany.
- Acute hematological conditions: Acute hemolytic anemia, sickle cell crisis, acute blood loss and bleeding episodes of coagulation defects.
- Acute digestive conditions: Severe gastroenteritis with dehydration.
- Fulminant infections as septicemia.
- Critical neonatal problems: Severe hyperbilirubinemia, respiratory distress, convulsions, septicemia and bleeding.

2. Observation and management of newly diagnosed chronic illness: When close observation, several investigations and changeable management are required, hospitalization becomes necessary. Some examples are:
- Newly diagnosed nephrotic syndrome.
- Newly diagnosed diabetes mellitus.
- Newly diagnosed epilepsy.

3. Observation and investigations of undiagnosed conditions: Some examples of these conditions are:
- Unexplained prolonged fever.
- Chronic anemia or chronic purpura of undetermined etiology.
- Hepatosplenomegaly of unknown etiology.
- Unexplained generalized oedema.
- Severe recurrent gastrointestinal hemorrhage.

Occasionally, hospitalization is made for **social reasons.** Parental anxiety may necessitate hospitalization of some illnesses that can be satisfactorily managed at home. Mild bronchiolitis, mild to moderate acute asthmatic attack and severe gastroenteritis are examples.

1

Neonatology

1. Routine Care of Normal Newborn.
2. Simple Infections.
3. Common Cutaneous Lesions.
4. Infantile Colic.
5. Gastroesophageal Reflux.
6. Low Birth Weight Baby.
7. Neonatal Convulsions.
8. Neonatal Respiratory Distress.
9. Septicemia and Meningitis.
10. Neonatal Jaundice.

1. Routine Care of Normal Newborn

Routine care of normal newborns should include the following aspects:

1. Care of the eyes, umbilicus and napkin area: It includes the following aspects:

(a) Eyes: Instill antibiotic eye drops, 3 times daily, for the first 4-5 days to prevent mucopurulent conjunctivitis.

(b) Umbilicus: Clean the umbilicus with alcohol, 3 - 4 times daily, up to 3 - 4 days following separation of the cord.

(c) Napkin area: Apply thin layer of a protective ointment to napkin area following each urination or defecation to prevent contact napkin dermatitis. Frequent change of wet diapers is also important.

2. Breast-feeding: It should be started 6-12 hours after delivery, to be given every 3 hours (or 2-4 hours) throughout the 24 hours (round-the-clock feeding). From the second month, a period of rest is taken from 12.00 midnight to 6.00 a.m. Sugary fluids or plain water may be offered between feeds especially during the first few days to prevent dehydration fever.

3. Orientation of the mother: Several problems may arise and mothers should know when to worry and when should not worry:

(a) Problems that are considered normal: The main problems are:

- Mild degree of nasal obstruction and snoring.
- Occasional regurgitation or vomiting (once or twice daily).
- Inverted sleep rhythm: Sleeping during day hours is usually better than during night. This is true up to the age of 2-3 months.
- Straining, even during sleep, is normal.
- Variable bowel movements: The normal average is 1-2 motions per day. However, passage of 5 -6 motions/day, often following each feed, is normal and not diarrhea. On the other hand, passage of one motion every 3-4 days is also normal and not constipation.

(b) Problems that necessitate medical consultation: The main problems are:

- Poor or absent suckling.
- Appearance of yellow coloration of eyes and skin.
- Appearance of whitish spots or patches on the tongue and oral mucosa.
- Significant repeated vomiting.
- Rapid or difficult respiration.
- Fever.

(c) Weight gain: normally, the newborn does not start to gain weight except after the first 7 - 10 days. The normal rate of weight gain is about 200 gm/week.

2. Simple Infections

1. Mucopurulent conjunctivitis

Instillation of an antibiotic eye drops, 3-4 times per day, for 5 days is usually sufficient. In severe cases, eye drops can be used up to 8 times/day, and an antibiotic eye ointment can be used at night. Frequent eyewash with saline or boric acid lotion is important.

* Prescription:

RI Boric acid lotion 2%.
Eyewash, several times/day.

RI Iso-Miphenicol OR Isopto-Fenicol
Instill 1 - 2 drops, in each eye, 3 - 4 times/day, for 5 days.

+ In severe cases, add:

RI Garamycin OR Gentamicin eye ointment.
Apply once at night, for 2 days.

2. Oral moniliasis

Local application of an antifungal drug as nystatin ***(Mycostatin or Fungistatin)*** or miconazole ***(Daktarin, Miconaz or Micazole)*** for one week is usually sufficient. Other monilial infections, especially monilial napkin dermatitis should be excluded and monilial infection of the mother's nipples, if present, should be also treated.

* Prescription:

RI Mycostatin OR Fungistatin oral suspension (100.000 unit/ml).
One dropper (1 ml) ... oral (drop by drop) ... every 6 hours ... for 7 days.

OR

RI Daktarin OR Miconaz OR Micazole oral gel 2%.
1/4 spoon (included) ... oral ... every 6 hours ... for 7 days.

- For napkin dermatitis, see below.
- For monilial sore nipple, see breast-feeding.

3. Umbilical sepsis

Evaluation of the general condition and suckling power is important to exclude septicemia. Local cleaning of the area with alcohol several times per day may be sufficient. An oral antibiotic as erythromycin or cephalexin for 5 days may be used in severe cases.

3. Common Cutaneous Lesions

1. Napkin dermatitis

In mild cases, application of a protective ointment as zinc oxide following each urination or defecation is usually sufficient. A topical steroid cream (as ***Dermatop or Perderm cream),*** applied twice daily is usually needed in moderate and severe cases. With superimposed monilial infection, a topical steroid and antifungal cream, twice daily, should be used ***(Kenacomb, Sicorten-plus, Daktacort, Micosone, Pevisone, Triderm, Polyderm, Lotriderm or Quadriderm cream).*** Duration of therapy is usually 4-7 days. Frequent change of wet diapers and avoidance of irritating soaps are important. In severe wet lesions, tight diapers should be avoided to allow air-drying (see topical medications).

2. Seborrheic dermatitis

Cradle cap of the scalp is the most common form in neonatal period and infancy. Topical application of a steroid ointment ***(Elecon or Diprosone ointment)*** or a steroid and salicylic acid ointment ***(Locasalen or Saligesic ointment),*** twice daily, for 5 - 7 days is usually sufficient. Wet compresses to moist and fissured lesions and gentle removal of the crusts, prior to steroid application, are important (see topically-applied medications).

3. Umbilical granuloma

Local application of absolute alcohol, several times per day is usually effective. Large or persistent granuloma for more that 10 days requires a careful cauterization of the granuloma tissue, with silver nitrate ***(Silver nitrate 5%),*** once or twice daily till the base becomes dry (usually over one week). Care should be taken to avoid burning of the surrounding skin. A cotton-tipped applicator can be used for the strict cauterization of the granuloma tissue.

4. Infantile Colic

Diagnosis of infantile colic should be only made after exclusion of other causes of crying. Physiological causes as underfeeding, faulty feeding, wet diapers, too much clothes or tight binders should be excluded, and pathological causes as otitis media, septicemia, inguinal hernia and severe napkin dermatitis should be also ruled out. Management includes 3 basic aspects:

1. Simple instructions: Mothers should know the followings:

- During the attack, holding the baby upright or in prone position across the mother's lap may be helpful.
- During feeding, the baby should eructate twice, at the middle and the end of feeding. Swallowing air is frequently responsible.
- The mother should avoid foods that may cause distress to the baby as spices and chocolate.
- Happiness and relaxation of the mother are also important.

2. Drugs: Although there is no magic drug that can prevent the attacks, **spasmolytics and sedatives** may be helpful in severe cases characterized by prolonged attack over several hours. The most suitable preparations contain both a spasmolytic (pipenzolate) and a sedative (phenobarbitone), as:

RI Spasmotal OR Babytal OR Piptal drops.
2 drops/kg/dose ... oral ... during the attack.
or 2 drops/kg/dose ... 3 - 4 times/day, 30 minutes before feeding.
(As the attacks are principally at night, the 3 doses can be given during the evening and night hours).

Other drugs as **antiflatulents** may be used to decrease colic due to gases. The mainly used drug is simethicone.

RI Simethicone OR Baby rest OR Dysflatyl OR Flatidyl drops .
Dosage is 10-15 drops 1-3 times per day.

3. Reassurance: Mothers should be reassured that the condition does not reflect any serious illness. It may increase in severity to reach its peak at the age of 6 weeks and it will subside gradually to disappear at the age of 3 month.

Notice: Some available preparations in the market are made of tincture belladonna (as a spasmolytic) and potassium bromide (as a sedative). However, bromides are now obsolete in medicine and should not be used especially in children as they may cause nightmares, night screaming and somnambulism (walking during sleep). Some of these preparations are:

RI Walirine OR Sedocal syrup.
RI Aqua Baby syrup.

5. Gastroesophageal Reflux

The possibility of gastroesophageal reflux should be considered in case of persistent regurgitation or vomiting in neonatal period or early infancy. Other medical and surgical causes of neonatal vomiting should be thoroughly excluded (see Pediatric Clinical Diagnosis). It is important to mention that accurate dietetic history and evaluation of growth are important. When the infant is overweight for his age and sex, the persistent vomiting is mostly caused by overfeeding.

Management of gastroesophageal reflux includes the following aspects:

1. Simple instructions: They may be useful in mild cases even without addition of any drugs:

(a) Eructation: Let the baby eructate twice, at the middle and the end of feeding, as swallowed air may be partially responsible.

(b) Positioning: After feeding, keep the baby in prone position with 30-degree elevation of the head, for one hour. Positioning will minimize the reflux of gastric contents into oesophagus.

(c) Thickened formula: In artificially fed infants, the formula can be thickened by adding one spoon of any of the commercially available cereals or rice preparations as ***Rizini Rice or Cerelac Rice.*** (See nutrition).

These simple measures should be tried first for 1 - 2 weeks before prescribing any medication.

2. Drugs: They are indicated in moderate to severe cases and when simple measures alone are not effective:

(a) Antiemetics: Metoclopramide is the mainly used drug because of its gastro-kinetic effect (enhances gastric emptying). It is given orally in a dose of 0.5 mg/kg/day, in 3 - 5 divided doses, 30 minutes before feeding. It is important to remember that the concentration of the drug in various available preparations is different ***(Primperan drops, 2.5 mg/ml or Plasil drops, 4mg/ml).*** For practical dosage, see below.

(b) H_2 receptor antihistamines: Cimetidine may be added in severe cases to reduce the gastric acidity. It is given orally in a dose of 40 mg/kg/day, in 3 - 4 divided doses, before feeds ***(Tagamet syrup, 200 mg/5 ml).***

(c) Antacids: They are also used in severe cases to neutralize gastric acidity to prevent esophagitis. Aluminium hydroxide gel is given orally in a dose of 2 ml before each feed ***(Epicogel OR Mucogel OR Alkasilone suspension.).***

Most cases of gastroesophageal reflux respond to simple measures and drugs. Signs of response include adequate weight gain and diminished vomiting and regurgitation.

3. Surgery: It is only indicated in exceptionally severe cases characterized by recurrent aspiration and weight loss, and when adequate trial with drugs for 10 weeks is not effective. Radiological studies, prior to surgery, are essential to differentiate the condition from other causes of recurrent aspiration as crico-pharyngeal incoordination and H-type of tracheoesophageal fistula.

Practical dosage

OR ***RI Primperan drops (2.5 mg/ml).***
One drop/kg/dose ... oral … 30 minutes before feeding … 4 times/day.

OR ***RI Plasil drops (4 mg/ml).***
One drop/kg/dose ... oral ... 30 minutes before feeding ... 3 times/day.

In severe cases, add:

RI Tagamet syrup (200 mg/5 ml).
One ml/kg/day ... oral ... divided into 3 - 4 doses.

RI Epicogel OR Mucogel OR Alkasilone OR Alkomag suspension.
Two ml ... before feeding ... 4 - 6 times/day.

6. Low Birth Weight Baby

Management of low birth weight babies depends mainly on the birth weight, degree of prematurity and the general condition, especially the suckling power.

A) Routine care

Most babies with birth weight above 2000 gm are in good condition and have a good suckling power. In absence of any critical illness necessitating hospitalization, these babies can be sent home and managed as the normal newborns.

B) Incubator care

It is indicated for babies with birth weight below 2000 gm and for many larger ones with any critical illness as convulsions, respiratory distress, deep jaundice, septicemia or bleeding. Incubator care includes the following aspects:

1. Temperature: The incubator temperature should be adjusted to keep the body temperature within normal values (36.5 - 37.5°C). The optimal incubator temperature, suitable for different body weights is:
- 35°C (for babies below 1000 gm)
- 34°C (for babies between 1000 - 1500 gm)
- 33°C (for babies above 1500 gm)

Higher or lower values may be needed according to the condition.

2. Humidity: The optimal humidity, which keeps the body temperature, is usually between 40 - 60%.

3. Feeding: The used method depends on the birth weight, suckling power and presence or absence of complications:

(a) Bottle-feeding: It is indicated in vigorous infants with birth weight above 1500 gm. Expressed mother's milk or humanized formula can be used. Feeding is given every 3 hours throughout the 24 hours (8 feeds/day). The amount can be increased gradually according to the condition. Bottle-feeding is contraindicated in presence of any critical illness as convulsions or respiratory distress.

(b) Nasogastric tube feeding: It is indicated in infants with birth weight below 1500 gm and in larger ones with poor suckling power. It is also indicated to replace I.V. fluids in infants with critical illness.
- Milk used: Humanized formula or low birth weight formula.
- Concentration: Full strength formula can be used in infants above 1500 gm and a diluted formula (1/2 strength) can be used for one or 2 weeks in infants below 1500 gm.
- Frequency of feeding: Infants above 1500 gm can be fed every 3 hours.

Two-hourly feeding is used in those between 1000 - 1500 gm and feeding every hour for infants below 1000 gm.

- Amount/feed: It depends on the birth weight and the infant's tolerance. The principal rule is to proceed slowly and gradually. The total daily intake should be about 150 - 200 ml/kg at the age of 10 - 14 days.

The following suggested schedule could be used.

		Below 1000 gm	1000 - 1500 gm	Above 1500 gm
Type of milk		low birth weight.	low birth weight.	Humanized.
Concentration		Diluted for 2 weeks.	Diluted for one week.	Undiluted.
Frequency		Every hour.	Every 2 hours.	Every 3 hours.
Amount/ feed	Day 1	1 ml.	3 ml.	4 ml.
	Day 2	2 ml.	5 ml.	8 ml.
	Day 3	3 ml.	7 ml.	12 ml.
	Day 4	4 ml.	9 ml.	16 ml.

- The first 2 - 3 feeds should be distilled water (as a test for tolerance).
- The amount can be increased or decreased according to response.
- Vomiting or abdominal distension is an indication to reduce the amount.
- Try oral feeding when the infant's weight exceeds 1500 gm.

(c) Total parenteral nutrition: It is only indicated in very low birth weight infants when tube feeding is not tolerated and also in those with serious intestinal diseases as necrotizing enterocolitis. Total parenteral nutrition should be only made in neonatal intensive care units and with experienced personnel. (See nutrition).

4. Oxygen therapy: It is only indicated in presence of cyanosis, apnea, respiratory distress or brain insult. Oxygen should be used with the lowest possible concentration and for the shortest possible time. (For details, see oxygen therapy).

5. Antibiotic therapy: It is only indicated in presence of serious infections as septicemia, pneumonia or meningitis. However, prophylactic antibiotic therapy may be used in very low birth weight infants below 1000 gm. With any clinical suspicion of septicemia, a combination of ampicillin and gentamicin, I.V., is a good initial therapy. A third-generation cephalosporin as cefotaxime may be added in severe cases (See septicemia).

6. I.V. fluid therapy: It is only indicated in presence of critical illness as convulsions, respiratory distress or serious infections. The I.V. fluid therapy in prematures is as follows:

- First day: 75 ml/kg/day .... of glucose 10%.
- Second day: 90 ml/kg/day ... of maintenance solution (glucose 10% and saline in a ratio of 4:1 with addition of 1 ml of potassium chloride 15% to each 100 ml of the solution and 2 ml/kg of calcium gluconate 10%).
- Third day: 100 ml/kg/day of the same maintenance solution.
- Then: Increase 10 ml/kg every day to reach 150 ml/kg/day.

If I.V. fluid therapy is necessary for more than 3 - 4 days, nasogastric tube feeding should gradually replace the I.V. fluids.

7. Phototherapy: It is indicated in presence of clinically evident jaundice to keep serum bilirubin level below the critical values. Exchange transfusion is indicated when serum bilirubin level approaches the critical level for weight and condition (see neonatal jaundice).

8. Vitamin and iron supplementation: It is usually indicated in low birth weight infants at the age of 2 weeks e.g.:

RI Enfa-vit OR Bebe-vit OR Polyvital drops: 5 drops once daily.
RI Fer- in-sol drops: 5 drops once daily.

9. Monitoring of growth: Daily weighing of the infant is important. Weight gain is usually not achieved before the age of 10 - 14 days. Daily weight gain of 20 - 40 gm is satisfactory.

10. Termination of incubator care: The main criteria for discharge are:

- Weight above 2000 gm (or at least 1800 gm).
- Good suckling power and adequate oral intake (150 ml/kg/day).
- Preserved body temperature (outside the incubator).
- Absence of any critical illness.

7. Neonatal Convulsions

Management of neonatal convulsions includes the following aspects.

1. Correction and exclusion of metabolic causes: Blood sugar level, serum calcium, serum magnesium and serum sodium should be measured in every case of neonatal convulsions:

- Hypoglycemia: 1 - 2 ml/kg of glucose 25% … I.V. over 1 minute.
- Hypocalcemia: 2 ml/kg of calcium gluconate 10% ... I.V. over 10 minutes.
- Hypomagnesemia: 2 ml/kg of magnesium sulfate 10% ...I.V. over 20 minutes.
- Hyponatremia: 5 ml/kg of sodium chloride 3% ... I.V. over 20 minutes.

2. Control of convulsions and prevention of further fits: The mainly used drugs are Phenobarbital and phenytoin.

- Phenobarbital: Loading dose: 10-15 mg/kg ... I.V. over 3 minutes.
  Maintenance: 3 mg/kg/dose ... I.V. every 12 hours.

When phenobarbital is not effective, add:

- Phenytoin: Loading dose: 10-15 mg/kg … I.V. over 5 minutes.
  Maintenance: 3 mg/kg/dose ... I.V. every 12 hours.

Maintenance anticonvulsant therapy may be continued for several days and until recurrence becomes unlikely. Withdrawal should be gradual.

3. Reduction of increased intracranial pressure: The following measures are important to reduce the increased intracranial pressure:

- Raise the head 30° to increase cerebral venous drainage.
- Fluid restriction: Give only 60 - 70% of total daily requirements.
- Drugs: Dexamethasone: 0.5 mg/kg/day ... I.V. in 2 divided doses.
  Furosemide: 1 - 2 mg/kg/dose ... I.V. It may be repeated.
- In severe cases with impending or frank herniation, mechanical ventilation is used to induce hyperventilation to keep $PaCO_2$ just below 30 mm Hg. CO_2 wash is useful to decrease cerebral blood flow and intracranial pressure (see comatose child).

4. Preservation of cerebral functions: Oxygen and glucose are essential for cerebral functions:

- Give oxygen 40% till the baby becomes fully conscious.
- Maintenance I.V. fluids should contain glucose 10%.
- Nasogastric tube feeding should be initiated from the second day even if the patient is still comatose. Oral feeding is only resumed after the patient becomes fully conscious.

5. Surgical intervention: It may be indicated in selected cases of intracranial hemorrhage. Neurosurgical consultation is important.

8. Neonatal Respiratory Distress

Any neonate with respiratory distress should be admitted to a neonatal intensive care unit, where facilities for assisted ventilation are available.

Urgent chest x-ray is important to exclude conditions necessitating urgent intervention as pneumothorax and diaphragmatic hernia. Radiological findings of other conditions as hyaline membrane disease or pneumonia may be also evident.

Management of hyaline membrane disease or severe pneumonia includes the following aspects:

1. Incubator care: Temperature should be adjusted to keep the body temperature between 36.5 - 37.0°C. Humidity of 50 - 60% is required.

2. I.V. fluid therapy: It is indicated to provide the daily requirements of water, electrolytes and calories.

- First day of life: 75 ml/kg/day of glucose 10%
- Second day: 90 ml/kg/day of maintenance solution.
- Third day: 100 ml/kg/day of maintenance solution.

Then the amount is increased (10 ml/kg/day) up to a total daily intake of 150 ml/kg/day. (See low birth weight).

3. Correction of hypoxemia and CO_2 retention: The principal goal in management of hyaline membrane disease is to support the respiratory functions for 3-4 days until spontaneous recovery occurs. Continuous monitoring of respiratory rate, heart rate and arterial oxygen saturation (with pulse oximeter) is important and repeated measurements of arterial blood gases (PaO_2, $PaCO_2$ and pH) are essential especially with moderate to severe disease.

(a) Oxygen therapy: It is the main line of therapy and it is given to keep arterial saturation above 90% and PaO_2 between 60 - 80 mmHg.

- ***Method:*** Inside the incubator or with a head box.

- ***Concentration:*** It depends on the severity of illness:

(a) In cyanosed infant, give 100% oxygen (with mask) to relieve cyanosis and decrease gradually (over few hours) to 40-60%.

(b) In absence of cyanosis, start with 40-60% oxygen and then adjust the concentration to keep arterial oxygen saturation above 90%(with pulse oximeter). Repeated blood gases are important for proper management.

* If saturation is above 90% and PaO_2 is 60-80 mmHg, maintain on 40-60%.

* If saturation is below 90% and PaO_2 is below 50 mmHg with 70% oxygen, continuous positive airway pressure or mechanical ventilation are indicated.

- ***Duration:*** Oxygen therapy is usually needed for about 3 - 7 days. Gradual withdrawal (5 - 10% decrements/time) is important.

(b) Continuous positive airway pressure (CPAP): It is indicated when PaO_2 is below 50 mmHg or oxygen saturation is below 90% with 70% oxygen.

- Method: With nasal catheter or through endotracheal tube.
- Pressure: Start with 5 mmH_2O and 70% oxygen. If PaO_2 is still below 50 mmHg, increase pressure to 7 or 8 mmH_2O and oxygen to 80 or 90%.
- If CPAP with pressure 8 and oxygen 90% are not effective to relieve hypoxemia, assisted ventilation is indicated.

(c) Assisted ventilation: It is indicated in the following conditions:

* If pH is below 7.15 or $PaCO_2$ is above 60 mmHg.
* If PaO_2 is below 50 mmHg with CPAP.
* Frequent apnea in spite of oxygen, CPAP and aminophylline therapy.

Assisted ventilation can be made with either:

* Intermittent ventilation with bag and mask for 5 minutes every 20 minutes.
* Mechanical ventilation.

4. Antibiotic therapy: Parenteral antibiotic therapy is indicated since differentiation between hyaline membrane disease and pneumonia may be difficult. A combination of ampicillin and gentamicin for 7 - 10 days is usually sufficient:

- **Ampicillin:** 50-100 mg/kg/dose ... I.V... every 12 hours.
- **Gentamicin:** 3 mg/kg/dose ... I.V... every 12 hours.

In severe cases, gentamicin may be substituted with a more potent aminoglycoside (amikacin) and a third-generation cephalosporin (as cefotaxime) may be added. New antibiotics as imipenem ***(Tienam vial)*** may be also considered.

5. Surfactant therapy: It may be used in very low birth weight infants with a severe hyaline membrane disease. It is given through an endotracheal tube in a dose of 5 ml/kg and the dose may be repeated after 12 hours if the response is inadequate. The available preparations ***(Exosurf vial OR Survanta suspension)*** are very expensive.

6. Treatment of associated complications: Especially:

- Metabolic acidosis: 3 ml/kg of sodium bicarbonate 5% ... slow I.V.
- Anemia: Small fresh transfusion (10 ml/kg) may be needed.
- Shock: Inotropic drugs as dopamine may be used.

7. Feeding: Tube feeding can be started from the third day even in mechanically ventilated infants and the amount can be increased gradually according to the tolerance. The total daily intake (I.V. fluids and tube feeding) should be around 120 - 150 ml/kg. Change to oral feeding is only initiated after discontinuation of oxygen therapy.

9. Septicemia and Meningitis

Management should include the following aspects:

1. Hospitalization: With clinical suspicion, the baby should be hospitalized, preferably in a neonatal intensive care unit. Repeated evaluation of vital signs, level of consciousness and suckling power is important.

2. Antibiotic therapy: It is the principal line of therapy. It should be started immediately without waiting for results of investigations.

- Initial parenteral combined therapy with ampicillin (100 mg/kg/day, I.V. divided into 3-4 doses) and gentamicin (5-7 mg/kg/day, I.V., divided into 2-3 doses) is satisfactory. Ampicillin can be substituted with other broad-spectrum penicillins with antipseudomonal activity as piperacillin and gentamicin may be also substituted with other aminoglycosides as tobramycin or amikacin. In severe cases, a third-generation cephalosporin as cefotaxime (100 mg/kg/day, I.V. in 2 divided doses) may be also added. When the possibility of anaerobic infection is considerable, metronidazole (7.5 mg/kg/dose, I.V. every 8 hours) can be used.

- Subsequent change of antibiotic therapy can be made according to the results of culture-sensitivity studies. Ceftazidime (100 mg/kg/day, I.V. in 2 divided doses) is the drug of choice for pseudomonas infection and vancomycin (40-60 mg/kg/day, I.V. in 3-4 divided doses) is the drug of choice for staphylococci. Newer antibiotics as imipenem (60-100 mg/kg/day ... I.V. infusion) may be also considered.

- The minimum duration of antibiotic therapy is 2 weeks in septicemia and 3 weeks in meningitis. As a rule, antibiotic therapy should be continued for 5-7 days after apparent clinical cure.

3. Fresh blood transfusion or exchange transfusion: It is used in severe cases especially when complicated with DIC.

4. Intravenous immunoglobulins may be also considered. The dose is 300 mg/kg, I.V. infusion (over 6-8 hours), daily for 5 days (see immunological products).

5. Treatment of complications: The main complications of severe septicemia are septic shock, septicemic renal failure and DIC. Prompt management of any complication, when present, is important.

6. Feeding: The suitable method depends on the condition:

- Bottle-feeding or breast-feeding: In infants with good suckling power.
- Tube feeding: In those with poor suckling.
- I.V. fluids: In presence of complications.

10. Neonatal Jaundice

Management of neonatal jaundice depends mainly on the type (unconjugated or conjugated) as well as the cause.

A) Unconjugated hyperbilirubinemia

The main goal of therapy is to prevent kernicterus, which may occur when unconjugated serum bilirubin exceeds the critical level.

The **critical serum bilirubin level** at which kernicterus may occur depends on the birth weight and the general condition. It is:

* 20 mg/dl: For weight above 2500 gm.
* 18 mg/dl: For weight between 2500 - 2000 gm.
* 16 mg/dl: For weight between 2000 - 1500 gm.
* 14 mg/dl: For weight below 1500 gm.

(In sick neonates as those with acidosis, anoxia or septicemia, the critical level is 2 mg below the above-mentioned figures).

Repeated measurements of serum bilirubin level is important, especially when values near critical level are obtained.

In most cases of **physiological jaundice** in term infants, serum bilirubin level is quite below the critical level and the condition subsides spontaneously, without any therapy, over 5 - 7 days.

1. Exchange transfusion: It is mainly indicated in severe hemolytic disease due to Rh incompatibility. The idea is to remove the excess bilirubin as well as the maternal antibodies responsible for hemolysis. In severe hemolytic disease, exchange transfusion is indicated in the following conditions:

(a) Cord bilirubin above 5 mg/dl or hemoglobin below 10 gm/dl.
(b) Rapid rise of serum bilirubin (more than 1 mg/hour).
(c) Serum bilirubin exceeding the critical level (see above).
(d) Clinical signs suggesting kernicterus at any serum bilirubin level.

The blood used for exchange should be fresh and preferably of group O, Rh negative. The infant's blood group, Rh negative may be used as an alternative.

The procedure is carried out through an umbilical vein catheter, where alternating aspiration of 20 ml of infant blood and infusion of 20 ml of donor blood is made. The amount of blood used equals the double blood volume of the infant (2 x 85 ml/kg). The whole procedure should be carried out over one hour.

After exchange transfusion, repeated measurements of serum bilirubin every 6 - 8 hours is important. Phototherapy is usually needed after the first exchange to keep serum bilirubin below the critical level. However, a second or even a third exchange may be indicated in severe cases with rapidly rising bilirubin level.

2. Phototherapy: Exposure of the jaundiced skin to fluorescent light is effective in lowering the unconjugated serum bilirubin level. Skin bilirubin absorbs light and unconjugated bilirubin is converted into unconjugated isomers that are excreted in bile and urine. The main indications of phototherapy are:

(a) Following exchange transfusion to minimize the number of subsequent transfusions.

(b) In premature infants with clinical jaundice to keep serum bilirubin below critical levels.

(c) In term infants with exaggerated physiological jaundice or hemolytic disease due to ABO incompatibility, where values near critical levels are common. Unconjugated hyperbilirubinemia (above 15 mg/dl) is an indication.

Phototherapy should be continuous (throughout the 24 hours) with frequent change of position to ensure maximal skin exposure. Eyes and may be genitalia should be covered to prevent the harmful effect of light on these organs. Initial response to therapy is usually attained after 12 hours of exposure where values 1 - 2 mg lower than the initial values are usually obtained.

Repeated measurements of serum bilirubin can be made every 12 - 24 hours. Phototherapy should be continued until serum bilirubin becomes unlikely to reach critical levels. Values below 12 mg/dl in term infants can be considered as a criterion to discontinue phototherapy.

Phototherapy is generally safe. Loose stool, skin rash and hyperthermia may infants with mixed hyperbilirubinemia.

3. Phenobarbital: The use of phenobarbital (6 mg/kg/day) to enhance bilirubin conjugation and excretion is currently limited to rare conditions of persistent unconjugated hyperbilirubinemia as Crigglar Najjar syndrome.

B) Conjugated hyperbilirubinemia

Persistent elevation of conjugated bilirubin in the first month of life (neonatal cholestasis) is not uncommon. Regardless of etiology, clinical manifestations are usually the same and include jaundice, dark urine, pale stool and hepatomegaly. Identification of the cause is important, as management and prognosis are largely dependent on the causative disease. A laboratory approach is essential.

1. Management of treatable conditions: In small percentage of cases, neonatal cholestasis is caused by treatable conditions as galactosemia, septicemia or urinary tract infection.

1. Galactosemia: Dietetic management by lactose-free formula ***(Isomil milk).***
2. Septicemia: See above.
3. Urinary tract infection: Appropriate antibiotic therapy according to culture and sensitivity studies.

2. Management of extrahepatic biliary atresia: In another small group of cases, neonatal cholestasis is caused by extrahepatic biliary atresia. Early recognition of these cases by appropriate radio-isotopic studies (Hida scan) and liver biopsy is important because early surgical correction will prevent further hepatic injury and subsequent development of biliary cirrhosis. For patients with correctable lesion, direct drainage can be made, but in those with uncorrectable lesion, **Kasai operation** (hepatoporto-enterostomy) is carried out with a high success rate.

3. Management of neonatal hepatitis: Most cases of neonatal cholestasis belong to this entity. Congenital infections and metabolic conditions as tyrosinemia and alpha one antitrypsin deficiency are responsible for some cases. However, the great majority of cases are of unknown etiology (idiopathic or giant cell hepatitis) and the condition has both sporadic and familial varieties. In sporadic cases, about 70% of patients will recover over several weeks or months. Prognosis of familial cases is worse and recovery rate is as low as 20 %.

Whatever the cause of hepatitis, management is empirical and depends on the degree of hepatic injury and the associated complications:

(a) In early cases, some simple measures may be effective:

1. **Fat-soluble vitamins** (A, D, E and K) are needed to compensate for the inadequate absorption of these vitamins.
2. **Drugs to enhance bilirubin excretion: Phenobarbital** ***(Sominaletta syrup)*** in a dose of 6 mg/kg/day, oral, in 2 divided doses) and **cholestyramine** ***(Questran packets)*** in a dose of 120 mg/kg/dose ... oral, 3 times daily with feeds) may increase bile flow and help in elimination of retained bile acids and cholesterol. Cholestyramine (bile acid binder) has a constipating effect and increases malabsorption of fat-soluble vitamins. **Urso-deoxycholic acid** ***(Ursogall suspension and Ursogall OR Ursofalk capsules)*** is a secondary bile acid that can be used to enhance the excretion of conjugated bilirubin. It is given orally in a dose of 15 mg/kg/day as a single dose or 2 divided doses.
3. The use of **corticosteroids** (prednisone or prednisolone , 1-2 mg/kg/day ... oral) is controversial. However, it may be tried when other lines are ineffective.
4. With severe malabsorption and growth failure, **medium-chain triglyceride containing formulas** ***(Pregestimil formula)*** may be effective.

(b) In advanced cases with portal hypertension and liver failure, other additional measures are usually needed:

- Esophageal varices and bleeding can be controlled by repeated sclerotherapy or transthoracic ligation of bleeding varices. Shunting operations should be avoided. In presence of ascites, salt restriction, protein restriction and diuretics (furosemide 1 mg/kg/day) are indicated.
- Liver transplantation may be considered with a high success rate.

Practical example

An infant, 2 months old (5 kg) with chronic cholestasis.

1. Fat soluble vitamins

RI Enfa-vit OR Bebe-vit OR polyvital drops.
One dropper (1 ml) ... oral ... twice daily

RI Konakion OR Haemakion ampoule (10 mg).
One ampoule (1.M.), twice weekly.

2. Drugs to enhance bilirubin excretion

RI Sominaletta syrup (15 mg/5 ml)
One teaspoon … oral … twice daily.
OR
RI Sominaletta tablets (15 mg).
One tablet (crushed) …oral … twice daily.

RI Questran packets (4 gm, containing 1800 mg cholestyramine).
1/3 packet (600 mg), to be taken with feeds, 3 times daily.

RI Ursogall suspension (160 mg).
One teaspoon … oral … once daily.
OR
RI Ursogall OR Ursofalk OR Ursochol capsules (300 mg).
The contents of a 1/2 capsule are given orally, once daily.

3. Corticosteroids

RI Predsol OR Xilone syrup (5 mg/5 ml)
One teaspoon … oral … twice daily.
OR
RI Hostacorten tablets OR Hostacoten-H tablets (5 mg).
One tablet (crushed) …oral … twice daily.

4. medium-chain triglyceride containing formulas

RI Pregestimil milk.
4 scoops + 120 ml warm previously boiled water ... 6 feeds per day.

2

Nutrition

1. Problems with Breast-Feeding.
2. Formula Feeding
3. Infant Foods.
4. Tube Feeding.
5. Total Parenteral Nutrition (TPN).
6. Undernutrition.
7. Kwashiorkor.
8. Rickets.
9. Food Restriction in Disease.

1. Problems with Breast-Feeding

Breast milk alone is the ideal food for infants during the first 4 - 6 months and also up to the end of the first year in addition to other foods.

Some problems commonly arise and may threaten the continuation of breast -feeding. Clinicians should be oriented with these problems to provide a proper guidance.

1. Breast engorgement: It commonly occurs between 2-6 postpartum days due to failure of complete evacuation of the breast. Management is by:

- Frequent round-the-clock feeding.
- Hot compresses before feeding to improve milk flow.
- Cold compresses after feeding to prevent further congestion.
- Regular breast emptying by hand expression or breast pump to remove excess milk.

The condition usually subsides in few days.

2. Sore nipple: It begins on the second or third day where the mother feels pain during suckling. Management is by:

(a) Instructions

- More frequent nursing and for shorter periods.
- Start feeding on the less sore side.
- Change the position of the baby during feeding so that he grasps the nipple at different pressure points.
- After feeding, allow air drying of the nipples.

(b) Local measures

- Apply thin layer of lanolin cream after feeding.
- If pain is severe, apply local anesthetic cream 15 minutes before feeding ***(Lignocaine or Lignopanthen cream).***
- If monilia is associated, apply nystatin cream ***(Mycostatin cream),*** or any other topical antifungal cream, twice daily (see topically-applied medications).

The condition usually subsides over several days.

3. Twin delivery: In this case, the mother's milk will not be enough to feed both babies. Supplementary feeding is necessary with one of the humanized formulas where the breast and bottle are given to each baby alternatively.

4. Insufficient breast milk: When breast milk is not adequate and the baby is not growing at the expected rate, complementary feeding with one of the humanized formulas is necessary. If the infant is around the age of 4 months, weaning is started and the added food will compensate for the deficient amount.

5. Working mother: When the mother is obliged to leave the baby for several hours a day, supplementary feeding is necessary. The infant receives one or two feeds of humanized milk till the mother comes back. Again, if the infant is around the age of 4 months, weaning is started and the added feed is given while the mother is absent.

6. Pregnant mother: If the mother gets pregnant, breast-feeding can be continued up to the 7th month of pregnancy, provided the maternal diet is adequate and her general health allows.

7. Sick mother: In minor acute illness as upper respiratory tract infection or bronchitis, breast-feeding is continued and the mother should wear a mask during feeding to avoid cross infection. In more severe illness as febrile illness or pneumonia, breast-feeding is temporarily withdrawn until the mother recovers. In case of breast abscess, breast-feeding from the affected breast is temporarily withdrawn until recovery.

8. Maternal drugs: As lactating mothers frequently receive medications, it is very important to know what is serious and what is safe for the baby. Some simple rules are essential to avoid unnecessary withholding of breast-feeding:

- Most antibiotics are safe (except chloramphenicol and tetracyclines) so, penincillins, cephalosporins, aminoglycosides, erythromycin and metronidazole are safe.
- Most analgesics and antipyretics are safe in small doses (except ergot preparations and indomethacin), so aspirin, paracetamol and ibuprofen are safe in small doses.
- Vitamins B and C are safe, but A and D are serious.
- Hormones as insulin and small doses of steroids are safe, but iodides and oestrogen are serious.
- Sedatives, tranquilizers and antihistamines are safe in small doses, but serious in big doses.

2. Formula Feeding

Formula feeding (or bottle feeding) is *"feeding the human infant with milk formula or milk substitutes"*. The following 3 points are important:

1. When to use formula feeding (indications).
2. What type of milk to be used (types).
3. Program of feeding (number of feeds and amount per feed).

1. Indications of formula feeding

Although breast milk is the ideal food for infants, there are some situations in which breast milk is not sufficient or not appropriate. Formula feeding can be used in 3 ways (complementary, supplementary and substitutive feeding).

1. Complementary feeding: Where breast feeds are completed by bottle feeds. It is indicated when breast milk is not enough for normal growth (scanty breast milk secretion). Some precautions are important:

- Do not prescribe it at request, but be sure first that the mother's milk is not really enough, simply by assessing the rate of weight gain.
- The prescribed milk should be one of the standard humanized formulas.
- Breast milk should be given first, and then the feed is completed by the bottle.

2. Supplementary feeding: Where some breast feeds are replaced by bottle feeds. It is indicated in two conditions:

1. Twin delivery (where the mother's milk is not enough to feed both babies): So the breast and bottle are given to each baby alternatively.
2. Working mother (Where the mother is absent part of the day): During these hours, the baby can receive one or more bottle feeds.

3. Substitutive feeding: Breast-feeding is completely replaced by bottle-feeding. It is indicated in three conditions:

1. Absent breast milk secretion.
2. Sick mother with chronic illness as open T.B., heart failure or any other illness which makes the mother unfit to feed her baby. Maternal hepatitis B virus infection is not a contraindication to breast-feeding.
3. Sick infant as in some metabolic conditions where breast milk is not appropriate for the baby as in galactosemia and phenylketonuria.

2. Type of milk to be used

There are several commercially available formulas suitable for healthy or diseased infants. In most situations, the standard humanized formulas should be used. Special formulas for low birth weight babies and for particular disease states are also available.

1. Humanized milks: These formulas are modified to be very near to breast milk in composition and quality. Vitamins and iron, which are deficient in breast milk, are added. These formulas are the first choice for feeding healthy infants during the first 6 month when breast-feeding is inadequate or not available. The amount/feed is around 25 ml/kg.

* Available trade names are:

RI Jammet 1 milk OR Sunny Baby 1 milk OR Lactogen milk.

(The above 3 formulas are subsidized by the ministry of health and are much cheaper than the other formulas. The price is below 3 Egyptian pounds).

RI Nan 1 milk OR Bebelac 1 milk OR France lait 1 milk.
RI Aptamil 1 milk OR Biomil 1 milk OR Fabimilk 1 milk.
RI Frisovom milk OR Frisomil milk OR kingslac milk.
RI Delilac milk OR Mamilac milk OR Dialac M milk.
RI Bebelac EC (Extra Care) milk.
RI S-26 Gold milk
RI S-26 AR (Anti-Regurgitation) milk.

[All above formulas, except S-26 milks, have a small scoop (4 gm) and dilution is one scoop for 30 ml water. S-26 milks have a big scoop (8 gm) so dilution is one scoop to 60 ml water].

2. Follow-On milks: The protein content in these formulas is high (3gm/100 ml milk) compared to that in humanized milks (1.5 gm/100 ml). They are used in healthy infants above the age of 6 months to replace humanized formulas. They are also used in malnutrition where extra amount of proteins are required.

* Available trade names are:

RI Nan 2 milk OR Bebelac 2 milk OR France lait 2 milk.
RI Aptamil 2 milk OR Kingslac 2 milk.
RI Promil 2 Gold milk OR Primavita 2 milk.
RI Progress 3 Gold milk OR Milupa 3 milk OR Lacto 3 milk.

(Reconstitution of Promil is one to 60 ml , while the others are one to 30 ml).
(Progress 3, Milupa 3 and Lacto 3 milks are for children between 1-4 years old).

3. Full cream milks: These formulas can be used in healthy infants above the age of 6 months and in older children and adults. These formulas are not sweetened, so one teaspoon of sugar is added to each 100 ml of milk.

* Available trade names are:

RI Nido milk OR Milac milk OR Celia milk.

4. Low birth weight formulas: These formulas are used for premature infants with birth weight below 1500 gm. Once the birth weight exceeds 2000 grams, these formulas are replaced by humanized formulas.

* Available trade names are:

RI S-26 low birth weight milk.
RI Bebelac premature milk.

4. Hypo-allergic lactose-free (LF) formulas: In these formulas, the cow's milk is replaced by vegetable protein (soybean) and the lactose of milk is replaced by other sugars (sucrose or glucose). These formulas are mainly used in cow's milk allergy and lactose intolerance. Both conditions commonly follow severe cases of gastroenteritis, so they are commonly used in convalescent gastroenteritis. They are also suitable for dietetic management of galactosemia.

RI Isomil milk OR S-26 LF milk.
RI Dialac LF milk OR Bebelac LF milk.
RI Nursoy milk OR AL 110 milk.

(Reconstitution of Isomil and S 26 LF is one to 60, while others are one to 30).

5. Predigested or elemental formulas: In these easily digested formulas, the proteins are in the form of protein hydrolysate and the fats are present as medium-chain triglycerides. These formulas are used in malabsorption and intractable diarrhea due to pancreatic insufficiency or biliary insufficiency.

RI Pregestimil milk.

(Reconstitution of this formula is one to 30).

6. Phenylalanine-free formulas: they are used in dietetic management of phenylketonuria.

RI Lofenalac milk OR Phenyl-free milk.

3. Program of feeding

• **Number of feeds:** In complementary and supplementary feeding, the number of bottle-feeds is ranging from 1-6 feeds depending on the indication. In substitutive feeding, an average of 6 feeds per day are usually needed.

• **Amount per feed:** Calculation of the amount per feed can be made by one of two methods (age method and weight method). Age method is simple and can be used in healthy infants with appropriate weight for age. Weight method is more accurate and can be used for both healthy and diseased infants.

a) Amount per feed (in ml) according to age

- First month: 60-90 ml.
- 2-3 months old: 120-130 ml.
- 4-5 months old: 140-150 ml.
- 6-7 months old: 160-180 ml.

Calculated amount can be increased or decreased according to the infant's desire. The baby should not be forced to complete the calculated amount.

b) Amount per feed (in ml) according to weight

- The amount per feed equals 25 ml/kg.
- An infant one months old (4 kg) needs 4x25= 100 ml/feed.
- An infant 4 months old (6 kg) needs 6x25= 150 ml/feed.

Practical examples

1. Prescribe a formula for twins 1 month old. The breast milk is not sufficient to feed both babies.

RI Bebelac 1 milk OR Biomil 1 milk..

- Amount per feed = 90 ml = 3 scoops + 90 ml water.
- Number of feeds for each twin = 3-4 feeds (alternating with breast feeds).

2. Prescribe a formula for an infant 2 months old (5 kg). The breast milk secretion is very scanty or almost absent.

RI Nan 1 milk OR Aptamil 1 milk.

- Amount per feed = 120 ml = 4 scoops + 120 ml water.
- Number of feeds = 6 feeds per day.

3. Prescribe a formula for an infant 2 months old (5 kg). The mother returned back to her job from 8.00 am to 2.00 pm.

RI Mamilac milk OR Kingslac milk..

- Amount per feed = 120 ml = 4 scoops + 120 ml water.
- Number of feeds = Two feeds (at 9.00 am and 12.00 noon).

4. Prescribe a formula for an infant 2 months old (5 kg). The breast milk is not enough for normal growth.

RI Dialac M milk OR Delilac milk.

- Amount per feed = 60 ml = 2 scoops + 60 ml water (complementary feed to be taken after breast feeding). The amount can be increased to 3 scoops + 90 ml or 4 scoops + 120 ml according to the infant's desire.
- Number of feeds = 2-6 feeds per day.

5. Prescribe a formula for an infant 5 months old (6 kg) with secondary lactose intolerance following severe gastroenteritis.

RI 26 LF milk OR Isomil milk (Formulas with big scoop).

- Amount per feed = 150 ml = 2 and half scoops + 150 ml water.
- Number of feeds = 6 feeds per day.

OR RI Bebelac LF milk OR Dialac LF milk. (Formulas with small scoop).

- Amount per feed = 150 ml = 5 scoops + 150 ml water.
- Number of feeds = 6 feeds per day.

6. Prescribe a formula for an infant 7 months old (7 kg).

R/ Bebelac 2 milk OR Nan 2 milk OR Aptamil 2 milk OR Kingslac 2 milk.

- Amount per feed = 180 ml = 6 scoops + 180 ml water.
- Number of feeds = 2-3 feeds per day (in addition to 3 weaning feeds).

3. Infant Foods

A) Baby drinks

There is no scientific basis for use of these formulas. They are mainly formed of herbs as camomile and liquorice. Manufacturers claim that these herbs are useful for relieving colic and distension and for induction of calm sleep.
* Available preparations are:

RI Milupa herbal drink.
RI Riri herbal drink.
RI Milupa camomile drink OR Domaco camomile drink.

B) Weaning foods

These foods are used to replace some milk feeds from the age of 4 months onwards. The prescribed feed should be given with a spoon at a fixed time every day. The average amount given per feed is about 6 big spoons added to 150 ml water. The infant should not be forced to complete the prepared amount.

1. Cereal containing formulas: They are used at the age of 4 months to replace one milk feed.
* Available preparations are:

RI Cerelac Wheat.
RI Cerelac Wheat and milk.
RI Milupa 3 cereals.
RI Galactina Protocereal.
RI Galactina 5 cereals.

2. Vegetable containing formulas: They are used at the age of 5 months to replace another milk feed.
* Available preparations are:

RI Cerelac vegetables.
RI Gerber vegetables and chicken.
RI Gerber vegetables and Lamb.
RI Gerber vegetables and Beef.
RI Riri mixed vegetables.

3. Fruits containing formulas: They can be used at the age of 6 months to replace the third milk feed.
* Available preparations are:

RI Cerelac wheat and fruits.
RI Gerber mixed fruits.
RI Gerber Banana and Pineapple.
RI Riri mixed fruits.

C) Foods for severe gastroenteritis

These special preparations are used in severe cases of gastroenteritis. Some are useful to compensate for water and electrolyte losses, while others may be used in convalescent cases.

1. Oral rehydration solution: It is used in severe cases to prevent or treat dehydration. The contents of the packet are added to 200 ml of cold, previously boiled, water. The prepared solution contains: Sodium (90 mEq/liter), potassium (20 mEq/liter), Cloride (80 mEq/liter) and bicarbonate (30 mEq/liter).

* Available preparations are:

RI Rehydran packets.
RI Rehydro-zinc packets.
RI Hydro-safe packets.

The last 2 preparations have the advantage of lower sodium content.

2. Rice containing formulas: These formulas may be used in severe cases of gastroenteritis especially during convalescence. These preparations should not be used before the age of 4 months. If used, they can be given either separately or 1-2 spoons are added to the diluted milk formula. (See gastroenteritis).

* Available preparations are:

RI Cerelac Rice.
RI Galactina Rice.
RI Milupa Rice.

3. Carrot containing formulas: As rice preparations, these formulas are also used during convalescence of severe gastroenteritis. They also should not be used before the age of 4 months. If used, they are given either separately (one spoon to 90 ml water) or 1 - 2 spoons are added to the diluted milk formula.

* Available preparations are:

RI Milupa carrots and rice.
RI Riri carrots and rice.
RI Caroz carrots and rice.

4. Special complete formulas: These formulas are designed to provide all nutritional requirements during convalescence period of severe gastroenteritis. They can be used either in liquid or semisolid forms. These formulas are also not suitable before the age of 4 months.

* Available preparations are:

RI Milupa special formula.
RI Riri special formula.
RI Galactina special nutrition.

4. Tube Feeding

One of the golden rules in therapy is **"If the gastrointestinal tract is intact, use it".** For economic and physiological reasons, gastrointestinal feeding is the method of choice.

1. Indications of tube feeding

In pediatric practice, tube feeding is used in the following clinical situations:

- **Prematurity:** Most newborns with birth weight below 1500gm cannot suck vigorously and are in need of tube feeding (see low birth weight).
- **Severe anorexia:** As in severe complicated kwashiorkor.
- **Comatose patient:** If coma persists for more than 1-2 days, tube feeding is essential to provide the nutritional requirements.
- **Severe respiratory distress:** As in patients with bronchopneumonia or in those under mechanical ventilation. In these cases, if the distress persists for more than few days, nasogastric tube feeding should gradually replace I.V. fluids.
- **Severe bulbar paralysis:** In this case, oral feeding is hazardous may lead to serious aspiration.
- **Esophageal stricture:** In this case, tube feeding can be given through a gastrostomy tube.

2. Formulas of tube feeding

The used food depends on the age of the patient:

- **In prematures:** A humanized formula or a low birth weight formula can be used ***(S-26 low birth weight)***.
- **In infants:** A humanized formula is used and any of the weaning foods, mentioned before, can be also used.
- **In children:** A blendarized formula (home made or hospital made) can be used. These formulas are not expensive, so are suitable for prolonged use. There are commercial readymade formulas for tube feeding in children as:

(Ensure OR Ensure plus OR Pediasure complete formula).

3. Equipment and technique

A polyethylene nasogastric tube is inserted through one nostril into the stomach (tube size is French 5 or 6 in infants and French 8 in children).

- **Amount:** Start with a small volume (1/4-1/2 maintenance fluid requirements) and a diluted formula (1/4 - 1/2 strength), then increase volume and strength

gradually and according to tolerance. In infants the calculated amount is divided into 5 - 6 feeds and in children, 3 - 4 feeds per day are satisfactory.

- **Method of delivery:** The calculated feed is given either by infusion pump or put in an inverted bottle, connected to I.V. set, and allowed to advance by gravity. Alternatively, a big syringe (50 ml) can be used and a very slow injection through the nasogastric tube is made. In young infants and in those who cannot tolerate the intermittent feeding, continuous tube feeding can be made. The calculated amount per day is infused continuously throughout the 24 hours.

- **Evaluation of tolerance:** The tolerance to feeding is evaluated on the basis of gastric residuals before the next feed, stool character and presence of vomiting or abdominal distension.

- **Duration and termination:** Tube feeding can be continued as long as several weeks or months. The nasogastric tube should be removed every 3 - 4 days and a new one is inserted through the other nostril. Termination of tube feeding should be gradual with the concomitant increase in oral intake. Daily tube feeding and oral intake should be recorded to ensure that the total intake is adequate.

4. Complications of tube feeding

The main complications are:

- **Obstruction of the tube** by thick formulas or medications given through the tube. Irrigation after feeding or every 8 hours with water and saline is important.

- **Gastric retention** due to high caloric value or fat content of the used formula or due to the underlying disease. Antiemetic drugs as metoclopramide or domperidone can be used. In resistant cases, the nasogastric tube is advanced into the duodenum or jejunum (Nasoduodenal or nasojejunal feeding).

- **Diarrhea or abdominal cramps** due to thick hypertonic formula, medications given through the tube or bacterial contamination of the formula or the set used. A more diluted formula should be used and the set used is changed. Persistence of diarrhea after these measures should suggest mucosal atrophy, especially in malnourished patients, and total parenteral nutrition (TPN) should be considered.

5. Total Parenteral Nutrition (TPN)

Parenteral feeding through the I.V. route is possible and can provide the nutritional requirements necessary for metabolic maintenance, tissue repair and growth. TPN is a potentially serious procedure, so it should be only used when it is absolutely necessary and when a perfect cooperation between doctors, nurses and laboratory is available.

1. Indications of TPN

It is only indicated when oral and nasogastric feeding are not tolerated and when the expected time for gastrointestinal recovery is more than 7 days as in:

- **Severe prematurity** when nasogastric feeding is not tolerated.
- **Neonatal necrotizing enterocolitis** where gastrointestinal feeding is contraindicated for few weeks.
- **Severe protracted diarrhea** where all formulas are ineffective.
- **Major intestinal surgeries** as massive resection where oral feeding cannot be resumed before few weeks.

2. Solutions used

The main solutions used are:

- **Carbohydrates:** ***Glucose 10%.*** Each liter provides 100 gm glucose, i.e. each 10 ml/kg provides 1 gm/kg of glucose.
- **Fats:** ***Intralipid 10%.*** Each liter provides 100 gm fats, i.e. each 10 ml/kg provides 1 gm/kg of fats. Intralipid is a good source of energy. It provides the essential fatty acids in addition to phosphorus and vitamin E.
- **Proteins:** ***Vamin N, Totamine, Amino-venous or Pan-amino SG.*** Each liter provides 70 gm proteins in form of 18 aminoacids, i.e. each 10 ml/kg provides 0.7 gm/kg of proteins. It also contains electrolytes and each liter provides 50 mEq of sodium, 55 mEq of chloride, 20 mEq of potassium, 2.5 mEq of calcium and 1.5 mEq of magnesium. ***Vamin with glucose*** provides in addition 100 gm of glucose per liter and this allows decreasing the amount of water infused while increasing the amount of energy.
- **Electrolyte and trace elements:** ***Fed-el solution.*** It contains calcium, magnesium, chloride, iron, zinc, copper, manganese, fluorine and iodine. 4 ml of Ped-el are added to each 30 ml of Vamin with glucose.
- **Fat soluble vitamins:** ***Vitalipid infant.*** It provides vitamin A, D_2 and K1. It is added to Intralipid in amount of 1 ml/kg, but the total daily dose should not exceed 4 ml.
- **Water soluble vitamins:** ***Soluvit.*** The contents of the vial are dissolved in 5 ml glucose 10% and 0.5 ml of this solution is added to each 100 ml of glucose 10%. It contains vitamin B complex and vitamin C.

3. Dosage and technique

- **Three mixtures** are made:

- **Mixture 1:** Vamin with glucose + Ped-el: The dose is 30 ml/kg/day. This amount will provide 2.1 gm/kg of proteins in addition to the daily requirements of electrolytes and trace elements. It provides also 3 gm/kg of glucose. The total amount given per day should not exceed the adult dose (1000 ml).
- **Mixture 2:** Intralipid 10% + Vitalipid: The dose is 30 ml/kg/day. This amount will provide 3 gm/kg of lipids in addition to the daily requirements of fat soluble vitamins and phosphorous. The total amount given per day should not exceed the adult dose (1000 ml).
- **Mixture 3:** Glucose 10% + Solu-vit: 90 ml/kg in neonates and young infants and 60 ml/kg in older infants and young children.

- **Two I.V. lines** are needed:

- **Line 1:** It is used for Vamin and Intralipid infusion. There are 2 methods of infusion (the sequential and the simultaneous methods). In the sequential method, Vamin is infused over 8 hours followed by Intralipid over the next 8 hours. In the simultaneous method, both Vamin and Intralipid are infused simultaneously through separate infusion sets connected by a Y-shaped tap. No drugs should be injected through this line.
- **Line 2:** It is used for glucose 10% and Solu-vit mixture. The infusion is made throughout the 24 hours. Drugs can be injected through this line.

4. Precautions and monitoring

-**The calculated full dosage** of Vamin and Intralipid is reached gradually over several days. In the first day of therapy, start with 10 ml/kg of each and then increase the amount by 5 ml/kg/day until the full dosage is reached. During these days, the amount of glucose 10% is increased to compensate for the decreased total amount, e.g.

- **Day 1:** 10 ml/kg (Vamin) +10 ml/kg (Intralipid) + 130 ml/kg (glucose 10%).
- **Day 2:** 15 ml/kg (Vamin) + 15 ml/kg (Intralipid) + 120 ml/kg (glucose 10%).
- **Day 3:** 20 ml/kg (Vamin) + 20 ml/kg (Intralipid) + 110 ml/kg (glucose 10%).
- **Day 4:** 25 ml/kg (Vamin) + 25 ml/kg (Intralipid) + 100 ml/kg (glucose 10%).
- **Day 5:** 30 ml/kg (Vamin) + 30 ml/kg (Intralipid) + 90 ml/kg (glucose 10%).

- The solutions used and the I.V. tubing system should be changed every 24 hours to eliminate the risk of contamination.
- The I.V. catheters should be checked frequently and should be changed to other veins in case of thrombophlebitis.
- Body weight and fluid balance (intake and output) are recorded daily.
- Periodic laboratory investigations are essential. Serum electrolytes, blood sugar and plasma turbidity are checked every 2 days. If the plasma is

milky or markedly opalescent, the intralipid infusion should be discontinued. Osmolarity, liver functions (bilirubin and SGOT) and renal function (BUN and creatinine) should be checked every 4-5 days. After the first week of therapy, investigations can be made once a week.

5. Risks and complications

Several complications may arise with TPN:

- **Infections** from a local contamination or contaminated infusion may occur. Vigorous antibiotic therapy, guided by blood cultures, should be made.

- **Hyperglycemia and hyperosmolarity** may occur due to a high glucose load. When blood sugar exceeds 300 mg/dl, regular insulin can be used in a dose of 1 unit for each 100 ml glucose 10%.

- Liver functions may be impaired (**rising transaminases**) due to the high protein load, especially during the first week, but this usually subsides with continuation of therapy. With persistent elevation, Vamin infusion should be reduced.

- **Fever and acute chills** may occur during the first 12 hours of Intralipid infusion. Hepatic function may be impaired with the appearance of conjugated hyperbilirubinemia. Rarely, fever, jaundice, splenomegaly, and gastrointestinal bleeding may occur with intralipid infusion.

- With prolonged TPN, **deficiencies of trace elements** may occur.

6. Termination of TPN

Once the oral or the nasogastric intake becomes possible, TPN should be gradually discontinued over 2-4 days with the concomitant increase in oral intake.

Partial parenteral nutrition

In areas where facilities for TPN are not available, partial parenteral nutrition can be made and can provide satisfactory support for up to 2 weeks. A maintenance solution of glucose 10% and saline is made in a ratio of 4:1. For each 100 ml of this mixture, 1 ml of potassium chloride 15%, 2 ml of calcium gluconate 10% and 1 ml of magnesium sulphate 10% are added. Vamin with glucose and water soluble vitamins are also used:

- **Mixture 1** (glucose and electrolytes): 90 - 120 ml/kg/day.
- **Mixture 2** (Vamin and vitamins): 30 ml/kg/day.

5. Undernutrition

Chronic caloric deficiency secondary to undernutrition is a common nutritional disorder in underdeveloped countries. Poverty and ignorance are two important contributing factors.

The essential clinical manifestation of undernutrition is ***underweight*** for age and sex. Other clinical manifestations will depend on the degree of caloric deficiency:

- Mild caloric deficiency leads to slow growth ***(nutritional dwarfism).***
- Moderate caloric deficiency leads to ***nutritional failure to thrive.***
- Severe caloric deficiency leads to wasting ***(nutritional marasmus).***

(See Pediatric Clinical Diagnosis)

Management of undernutrition includes the following aspects:

1. Early detection of undernutrition: An alert physician should be able to diagnose undernutrition at early stages. Accurate **dietetic history** is extremely important. Dietetic errors as insufficient breast milk, diluted formulas or infrequent feeding can be detected by history. Periodic weighing of the infant to assess the rate of **weight gain** is important. Deviation from the normal rate (slow growth) or failure to gain weight can be early detected by regular periodic weighing.

2. Dietetic management: In early cases, treatment is simple by just correction of the dietetic error. In breast-fed infants, complementary feeding with a humanized formula is sufficient. In formula-fed infants, the proper concentration of milk and the adequate number of feeds will ensure a normal growth. In severe cases of marasmus, extra-caloric intake is necessary to compensate for weight loss. Initially, the volume of the prescribed milk should equal 200 ml/kg/day. The amount is then increased gradually to equal the amount for his expected weight. In weaned infants, high quality foods in adequate amounts are offered. Milk, yogurt, cereals, fruits, vegetable soup with minced chicken and eggs are the most suitable.

3. Treatment of complications: In severe cases complicated by serious infections as pneumonia or gastroenteritis, hospitalization is necessary as these infections may be the cause of death.

6. Kwashiorkor

Although protein deficiency is the basic nutritional factor in kwashiorkor, several vitamins and minerals are also deficient, so that the term **"multiple deficiency disease of childhood"** is recently suggested as the most appropriate term. Kwashiorkor is the commonest cause of acquired immunodeficiency in underdeveloped countries and the associated infections play an important role in maintaining protein, vitamin and mineral deficiencies.

Management of kwashiorkor varies according to the severity of illness as well as the type and severity of associated complications. The initial step is the clinical decision whether the case is for hospital or home management.

A) Home management of mild to moderate cases

In early and uncomplicated cases, successful home management is possible through correction of the dietetic error and supplementation of deficient vitamins and minerals:

1. Dietetic management: Foods that are responsible as sugary fluids, rice water and starch pudding should be discontinued and be replaced by a high protein diet.

(a) In breast-fed infants, breast-feeding should continue and a humanized formula ***(S-26 milk, Nan 1 milk, Bebelac 1 milk)*** is prescribed to compensate for protein deficiency (mixed feeding). It may be necessary to start with a diluted formula (1/2 strength) for several days to avoid gastrointestinal troubles. In infants with frequent diarrheas, prescribing a lactose-free hypo-allergic formula ***(Isomil or Nursoy)*** is recommended. The basic rule in successful dietetic management is to start with small-diluted amounts and to increase gradually the amount and concentration.

(b) In weaned infants or young children, prescribing high protein diet is important. Milk should be given twice daily. Other high protein foods as yogurt, ready-made cereals ***(Cerelac, Gerber Protocereal or Milupa 3 cereals etc.),*** vegetable soup with minced chicken and eggs are also offered daily. In low socio-economic classes, a cheap protein diet should be given as cottage cheese, broad beans, lentil and other legumes.

2. Vitamin and iron supplementation: Prescribing multivitamin drops ***(Enfa-vit or Bebe-vit drops)*** and iron drops ***(Fer-in-sol drops)*** are also important to compensate for the associated vitamin and iron deficiencies (see vitamin and mineral therapy).

B) Hospital management of severe cases

Hospitalization is indicated in presence of severe infections (as pneumonia or severe gastroenteritis), severe water and electrolyte disturbances (as dehydration and metabolic acidosis) and also in case of severe anorexia where the infant may refuse feeding totally.

Hospital management includes the following aspects:

1. Parenteral antibiotic therapy: Ampicillin (50 - 100 mg/kg/day, in 4 divided doses) and gentamicin (5-7 mg/kg/day, in 3 divided doses) are given I.V. for 7-10 days to control bacterial infections. Other antibiotics as cephalosporins may be added in severe infections.

2. Transfusion therapy: Whole blood transfusion (10-15 ml/kg) is indicated in presence of severe infection, severe anemia or severe anorexia. Plasma transfusion (10 ml/kg) or salt free albumin (5 ml/kg) is indicated in case of severe hypoalbuminemia.

3. Vitamin and iron supplementation: A daily multivitamin preparation is given ***(Enfa-vit drops or Bebe-vit drops)***. Iron is given orally in a dose of 2-6 mg/kg/day ***(Sytron syrup, 27 mg/5 ml).***

4. I.V. fluid therapy: Correction of dehydration, if present, is important. The I.V. fluids should provide more potassium to compensate for the commonly present hypokalemia. (See I.V. fluid therapy).

5. Dietetic management: Initial *nasogastric tube feeding* may be necessary in case of extreme anorexia. Diluted formula or hypo-allergic lactose free formula in small amounts may be initially used. The amount and concentration are increased gradually and according to tolerance. Once appetite improves, *oral feeding* can be started with the same rules applied for home management.

With clinical improvement (increased appetite, increased alertness and decreased edema), the patient can be discharged and managed as those of home management.

7. Rickets

A) Vitamin D deficiency rickets

Nutritional vitamin D deficiency rickets is the commonest type seen between 6 months and 2 years. Prolonged breast-feeding without supplementation with foods rich in vitamin D is the main cause. Frequently recurrent diarrheal illnesses are an important additional factor.

Management includes the following aspects:

1. Vitamin D therapy: This type is characteristically sensitive to vitamin D in ordinary therapeutic dosage. Vitamin D_2 or D_3 is given orally in a dose of 3000 - 5000 I.U./day for 3 - 4 weeks ***(Decal B_{12} syrup or Vitacal syrup or Calcical syrup, 1000 I.U./5 ml).*** As an alternative, a single intramuscular injection of vitamin D_2 or D_3 is equally effective and has the advantage of more rapid healing and less dependence on parents for daily administration ***(Devarol amp., 600.000 I.U/ml).*** Radiological signs of healing start after 2 weeks of onset (healing rickets) and become complete after 4 weeks (healed rickets). Failure of response to vitamin D after 4 weeks should suggest vitamin D resistant rickets.

2. Iron and calcium supplementation: In nutritional cases secondary to prolonged breast-feeding, associated iron deficiency anemia is quite common. Iron supplementation, at least in prophylactic dosage of 10 - 15 mg/day, is recommended ***(Fer-in-sol drops = 15 mg/ml).*** In proved iron deficiency anemia, a dose of 6 mg/kg/day of elemental iron for 8 weeks is given (see iron deficiency anemia). Calcium supplementation is not necessary in mild to moderate cases, but in severe cases, associated with hypocalcemia or complicated with tetany, oral calcium therapy in a dose of 40 mg elemental calcium/kg/day for 2 weeks is necessary ***(Calcium Sandoz syrup, 110 mg/5 ml).***

3. Simple instructions to parents: Correction of the dietetic error is important. Introduction of foods rich in vitamin D as egg yolk, meat or ready made fortified formulas is useful. Exposure to sunlight is helpful for vitamin D formation in the skin. Avoidance of weight bearing, especially in severe cases, is important to prevent deformities.

4. Treatment of complications: ***Tetany*** is urgently treated by I.V. calcium gluconate (10%) in a dose of 100 mg (1 ml)/kg. Injection should be slow over 5 - 10 minutes and monitoring of heart rate during injection is necessary. If the spasms or convulsions are not controlled, the dose can be repeated and phenobarbital is given I.V. or I.M. in a dose of 5 mg/kg. Oxygen therapy during the convulsive fit is important. After control of the attack, oral vitamin D and calcium therapy should be started. ***Deformities*** are mostly correctable with time. Persistent deformities may necessitate orthopedic consultation.

B) Vitamin D resistant rickets

When rickets does not respond to the ordinary therapeutic doses of vitamin D, the rickets is then called "vitamin D resistant" and some investigations are necessary to identify the causative disease:

- Serum calcium, phosphorus and alkaline phosphatase.
- Acid-base balance (for detection of metabolic acidosis).
- Evaluation of renal function (Blood urea and creatinine).
- Urine examination for phosphate excretion, glucosuria and aminoaciduria.

- *In familial hypophosphatemia,* serum phosphorus is low and urinary phosphate excretion is high. No aminoaciduria.
- *In hypocalcemic vitamin D dependent rickets,* serum calcium is low, serum phosphorus is normal or low. Aminoaciduria is present.
- *In renal tubular acidosis,* serum phosphorus is low, metabolic acidosis is present and renal function is normal.
- *In chronic renal failure,* serum phosphorus is high, metabolic acidosis is present and renal function is impaired.
- *In hypophosphatasia,* calcium and phosphorus are normal and alkaline phosphatase activity is low.

Management of vitamin D resistant rickets includes the following:

1. **Vitamin D therapy:** The oral use of activated forms of vitamin D is the treatment of choice. **One alpha hydroxycholecalciferol (alphacalcidol)** is given orally in a dose of 0.05-0.1 mcg/kg/day ***(One alpha drops, 0.1 mcg/drop),*** and is continued until healing occurs. Practical dosage is one drop/kg/day. If this very expensive drug is not available, **high doses of vitamin D_3** (2000 I.U./kg/day and may be up to 500.000 I.U./day) are used.

2. **Other lines of therapy:** It depends on the diagnosis:

- Familial hypophosphatemia: Oral phosphate supplementation (0.5 gm/day).
- Hypocalcemic vitamin D resistant: Oral calcium supplementation.
- Renal tubular acidosis: Oral bicarbonate therapy.
- Chronic renal failure: See chronic renal failure.

Practical example

1. Prescribe vitamin D for an infant with vitamin D deficiency rickets.

RI Decal B_{12} OR Calcical OR Vitacal syrup (1000 I.U vitamin D/5 ml).
One and half teaspoon, oral, 3 times daily for 3 weeks.

2. Prescribe vitamin D for 8-kg infant with vitamin D resistant rickets.

RI One alpha drops (0.1 mcg/drop)
8 drops, oral, one daily until healing occurs.

8. Food Restriction in Disease

It may be useful to review the diseases in which elimination of some foods plays an important role in management.

A) Diseases requiring special formulas

In these conditions, elimination of the responsible offending material is the main line of therapy:

1. Galactose-free diet: Indicated in galactosemia. Available preparations are Isomil milk, S-26 FL milk, Nursoy milk and AL 110 milk.

2. Lactose-free diet: Indicated in lactase deficiency whether congenital or following gastroenteritis. Available preparations are Isomil milk, S-26 FL milk, Nursoy milk and AL 110 milk.

3. Phenylalanine-free diet: Indicated in phenylketonuria. Available preparation is Lofenalac milk.

B) Diseases requiring avoidance of some foods

In these conditions, avoidance of certain foods is an important aspect of therapy:

1. Gluten-free diet: It is indicated in suspected or proved Celiac disease. All foods containing wheat or rye should be completely eliminated from the diet (see chronic diarrhea).

2. Low-protein diet: It is indicated in patients with acute or chronic liver cell failure and renal failure.

3. Low-fat diet: It is indicated in patients with fat malabsorption especially cholestasis.

4. Low-simple carbohydrate diet: It is indicated in management of type I diabetes. Simple carbohydrates as sugar, sweats, candies and carbonated beverages should be reduced (see diabetes).

5. Low-salt diet: It is indicated in patients with hypertension, heart failure, generalized oedema or chronic renal failure with volume overload.

6. Low-copper diet: It is indicated in patients with Wilson disease. Foods with high copper content as liver, chocolate and nuts should be avoided.

3

Infections

1. Simple Fever.
2. Typhoid Fever.
3. Other Bacterial Fevers.
4. Tetanus.
5. Diphtheria.
6. Scarlet Fever.
7. Measles.
8. Chickenpox.
9. Mumps.

1. Simple Fever

Acute febrile illness with no localizing signs (simple fever) is a quite common clinical presentation in pediatric practice. The diagnosis of simple fever or "nonspecific febrile illness" is made after careful ***clinical exclusion of focal infections*** (CNS, respiratory, cardiac, gastrointestinal, urinary etc.). Exclusion of early exanthems is also important.

In case of simple fever, the most important clinical problem is how to differentiate between viral and bacterial infections. Evaluation of the general condition by the **general clinical assessment** is very useful in this task. It is based on criteria gained by history and physical examination:

(a) History

1. Appetite and thirst.
2. Activity and playfulness.
3. Reaction to parents (the mood of the child).

(b) Examination

1. Level of consciousness: Does he look alert, drowsy, confused or comatose.
2. Appearance: Does he look healthy or sick (pale, toxic or shocked with hypotension, cold extremities and mottled skin).
3. Reaction to social stimulation: Does he smiles or looks anxious and irritable.

With this simple general clinical assessment, a skilled physician can often differentiate between 3 clinical entities, viremia, bacteremia and septicemia.

1. Viremia

The diagnosis of viremia is clinically made if the general clinical assessment reveals that the general condition is **fair**. The appetite and activity are not significantly affected and the patient is alert, does not look sick and reacts normally. In this case, management is by:

1. Antipyretics: Prescribing an antipyretic to lower the temperature is indicated when temperature exceeds 38°C or 38.5°C. Several drugs are available but **paracetamol** is the safest. It is given in a dose of 10 - 15 mg/kg/dose, oral, every 4 - 6 hours. Infants can receive the drop forms ***(Pyral or Abimol drops, 100 mg/ ml = 5 mg/drop),*** while children can use it as syrups ***(Pyral or Paramol syrup, 120 mg/5 ml)***. If the temperature is above 39.5°C and the patient is liable to vomit, the suppository form can be used (several concentrations are available). Alternatively, other antipyretics as **ibuprofen** ***(Brufen or Marcofen syrup)*** can be used. Both drugs (paracetamol and ibuprofen) are also available in one prepararion ***(Megafen syrup).*** **Acetylsalicylic acid** ***(Aspirin)*** should be avoided in infants and in viral illnesses because of the potential risk of Reye syndrome.

Other measures to lower the elevated temperature as tepid bath and sponges are also helpful but cold compresses with iced water should be avoided as it increases superficial vasoconstriction and may cause collapse. Excess fluid intake is also helpful. Parents should be instructed to respect the patient's appetite and not force the child to eat.

2. Re-examination: Re-examination after 24-48 hours is important. In up to 40% of cases, re-examination will reveal a focus of infection. If the patient in still febrile and the general condition is fair, reassurance is important as the illness will subside spontaneously over the next few days.

2. Bacteremia

The diagnosis of bacteremia is clinically made if the general condition is considerably affected and the patient looks **sick**. Management includes:

1. Simple investigations: Complete blood count (CBC) and C-reactive protein (CRP) are helpful. Leukocytosis above 15.000 cells/mm^3 with predominant segmented form (Polymorphonuclear leukocytosis) or a high band count above 10% (Bandemia) is highly suggestive of bacterial infection. Also, CRP level between 20-30 mcg/ml suggests bacterial infection.

2. Oral broad-spectrum antibiotic: When the investigations are not available or the patient cannot afford the expenses, it is reasonable to prescribe an oral broad-spectrum antibiotic as ampicillin or amoxicillin in a dose of 50 - 75 mg/kg/day for 5 days. The same treatment is applied to those with positive laboratory tests.

3. Antipyretics: The same drugs mentioned for viremia can be used. Aspirin can be used in children but not in infants.

4. Re-examination: Re-examination after 24 - 48 hours is important to search for a focus of infection and to evaluate the response to therapy. Persistent high fever above 39.5°C for more than 3 days in spite of antibiotic therapy may necessitate a change in antibiotic therapy where a second-generation cephalosporin (as cefaclor) may be used. Persistence of fever for more than 7 days (prolonged fever) is an indication for hospitalization and investigations.

3. Septicemia

The diagnosis of septicemia is clinically made in those with high fever (temperature above 39.5°C) and when general clinical assessment reveals that the patient is **seriously ill.** Poor activity, pallor, disturbed consciousness or shock (hypotension, cold extremities and mottled skin) is usually evident. In this case, management will include the following aspects:

1. Immediate hospitalization: It is necessary for observation, investigations and urgent management.

2. Urgent investigations: A blood sample is taken for CBC, CRP, ESR and blood culture, and a urine sample is sent for urine analysis and urine culture. CSF examination is also important to exclude bacterial meningitis and chest X-ray is needed to exclude pneumonia.

3. Urgent parenteral antibiotic therapy: Antibiotic therapy should start by the I.M. or preferably the I.V. route without waiting for the results of investigations. An initial combination of ampicillin (100 mg/kg/day, in 4 divided doses) and an aminoglycoside as gentamicin (5-7 mg/kg/day, in 2-3 divided doses) is satisfactory. The antibiotic therapy can be changed according to the clinical response and the results of cultures. A minimum duration of 10 days is usually necessary.

4. Control of high fever: With temperature above 39.5°C, tepid sponges and paracetamol given rectally are usually effective. In resistant cases or with hyperpyrexia (temperature above 41.0°C), I.V. acetylsalicylic acid is given in a dose of 10 - 15 mg/kg/dose ***(Aspegic injectable, 500 mg/5 ml).*** The dose can be repeated every 4 - 6 hours.

5. Treatment of septic shock: Inotropic drugs as **dopamine** and **dobutamine** are indicated to improve cardiac output. In severe cases, mechanical ventilation for "shock lung" should be considered. (See inotropic drugs and acute congestive heart failure).

6. Feeding: An initial maintenance I.V. fluid therapy may be necessary during the first few days. Oral intake is resumed as soon as the condition permits.

Practical examples

1. An infant, one year old (10 kg) with clinical diagnosis of viremia.

RI Pyral OR Paramol syrup (120 mg/5 ml)
One teaspoon, oral, when temperature exceeds 38.0°C, every 4 - 6 hours.

+ ***Re-examination after 24 - 48 hours.***

2. A child, 3 years old (15 kg) with clinical diagnosis of bacteremia.

RI Amoxil OR E-mox OR Hiconcil suspension (250 mg/5 ml)
One teaspoon (5 ml), oral, every 8 hours for 5 days.

RI Abimol syrup (150 mg/5 ml)
One teaspoon, oral, when temperature exceeds 38 .0°C, every 4 - 6 hours.

+ ***Re-examination after 24 - 48 hours.***

2. Typhoid Fever

Infection with salmonella typhosa is a common health problem especially in underdeveloped countries. Infection usually occurs through ingestion of contaminated foods or water. However, it may also occur from an infected patient or a chronic adult carrier.

Clinical manifestations are ranging from a mild disease to a severe septicemia. The possibility of typhoid fever is usually considered in patients presenting with a prolonged fever (fever with duration more than 7 - 10 days). Clinical examination may reveal splenomegaly and abdominal tenderness. All other causes of prolonged fever should be considered.

The suspected clinical diagnosis is confirmed by laboratory investigations. ***Blood culture*** is positive during the first week of illness in 40-60% of cases, while urine and stool cultures become positive from the second week. ***Polymerase chain reaction (PCR)*** is used to amplify specific genes of salmonella typhi in the blood of patients, which allows diagnosis within few hours. ***Widal agglutination test*** is the most commonly used investigation. A 4-fold rise in agglutinin titer or a rising titers in subsequent tests are diagnostic. Many false-positive and false-negative results occur and the diagnosis based on Widal test alone is subjected to errors.

Management of typhoid fever includes the following aspects:

1. Antibiotic therapy: **Chloramphenicol** (50 - 100 mg/kg/day) is the drug of choice. It can be given orally as a home management or I.V. in sick hospitalized patients. Duration of therapy is at least 10 - 14 days or for 5 days after the patient becomes afebrile. **Amoxicillin** (100 mg/kg/day, oral, in 4 divided doses) is equally effective and can be used as an alternative, especially with chloramphenicol-resistant strains. Ampicillin and co-trimoxazole are less effective and unreliable. In resistant cases, a **third-generation cephalosporin** as cefotaxime (200 mg/kg/day), ceftriaxone or ceftazidime (100 mg/kg/day) can be used parenterally (I.V. or I.M.).

2. Corticosteroids: Prednisone or dexamethasone (2 mg/kg/day, oral, in divided doses) may be used in patients with severe toxemia or prolonged fever, but only after several days of an adequate antibiotic therapy. Symptomatic improvement regarding the general condition and fever may be observed within few days. Duration of therapy should be as short as 3 - 5 days.

3. Antipyretics: Paracetamol or any other antipyretic is used for symptomatic control of fever. Temperature recording should be made before use.

4. Diet: In sick patients, excess fluids and soft diet are more tolerable. Once the appetite improves, ordinary diet can be offered. Supplementation of water-soluble vitamins (B and C) is recommended.

5. Health precautions: Parents should know that the patient is infectious through respiratory secretions, urine and stool during the period of illness. Hygienic precautions while dealing with urine and stool and strict hand washing are important. Stool culture for household adults may be considered to detect chronic carriers. Vaccination of siblings with typhoid vaccine (0.5 ml subcutaneous) may be considered.

6. Treatment of complications: Intestinal hemorrhage and perforation is an uncommon but serious complication. **Intestinal perforation** may occur late in the illness and is usually preceded by a fall in temperature. Marked increase in abdominal pain and tenderness with signs of peritonitis should suggest the diagnosis. Hypotension and rapid pulse are usually evident. Urgent plain x-ray on abdomen (erect position) is indicated and urgent surgical consultation is necessary. **Pneumonia,** if associated, is mostly caused by a superimposed infection with other organisms and appropriate antibiotic therapy is indicated. Other complications as pyelonephritis, endocarditis, septic arthritis or meningitis are rare.

7. Treatment of chronic carriers: Ampicillin or amoxicillin in high doses (100 mg/kg/day) for 4 - 6 weeks may be effective. In those with chronic cholecystitis, cholecystectomy is curative in the great majority of cases.

It is important to remember that typhoid fever is *not followed by permanent immunity* and re-infection may occur on further subsequent exposure.

Practical examples

1. A child, 3 years old (15 kg) with typhoid fever.

Rl Miphenicol OR Cidocetine suspension (125 mg/5ml).
2 teaspoons (10 ml), oral, every 6 hours for 10 -14 days (or 5 days after the patient becomes afebrile).

OR Rl Amoxil OR Hiconcil OR E-mox suspension (250 mg/5 ml).
One teaspoon (5 ml), oral, every 6 hours for 10 -14 days.

2. A child, 6 years old (20 kg) with typhoid fever. Temperature is 40.5°C and the patient looks seriously ill.

Hospitalization

+ *I.V. fluid therapy:* - Kadalex 1200 ml
- Saline 300 ml
over 24 hours (20 drops/minutes)
(To be replaced by oral feeding over the next 24 - 48 hours).

+ *Antibiotics:* - Chloramphenicol: 500 mg, I.V., every 6 hours for 10 -14 days.
OR - Cefotaxime: 2.0 gm, I.V., every 12 hours for 10 days.

+ *Antipyretics:* - Aspegic injectable: 2 ml (200 mg), I.V., to be repeated every 4 - 6 hours, when necessary.

3. Other Bacterial Fevers

Bacterial infections, other than typhoid fever, may be the cause of prolonged fever not responding to ordinary antibiotics. Diagnosis and specific therapy of these infections is important.

1. Brucellosis

Infection with brucella species usually occurs through contact with domestic animals. Ingestion of a contaminated milk, butter, cheese or ice cream is the usual source of infection. Suspected clinical diagnosis is confirmed by the *brucella agglutination test.* A titer above 1:160 is diagnostic. In children below the age of 8 years, a combination of **rifampicin** (20 mg/kg/day, oral, in 2 divided doses) and **co-trimoxazole** (8 mg of trimethoprim and 40 mg of sulphamethoxazole/kg/day, oral, in 2 divided doses) is the treatment of choice (see antibiotics and antituberculous drugs). In children above 8 years, tetracycline (30-40 mg/kg/day, oral, in 4 divided doses) is the treatment of choice.

2. Listeriosis

Infection with listeria occurs through inhalation or ingestion of milk from infected animals. Diagnosis is usually made by *positive blood cultures* because serological tests are unreliable. A combination of **ampicillin** and **gentamicin** is the most effective treatment. Treatment is for 10 - 14 days.

3. Tularemia

Infection with pasteurella tularensis in children occurs through ingestion of contaminated food (as rabbits) or water. Infection may also occur in children who have been bitten by infected flies, fleas, ticks or other hosts. The typhoidal form of tularemia resembles typhoid fever and is characterized by a protracted fever. *Tularemia aggulination test* is reliable for diagnosis. A titer of 1:80 or greater is positive. **Streptomycin** (30 - 40 mg/kg/day, I.M., in 2 divided doses) is the drug of choice. Duration of therapy is 7 - 10 days. Tetracyclines and chloramphenicol are also effective but relapses are common. Untreated tularemia may be serious and fatalities occur.

4. Tetanus

Infection with clostridium tetani usually follows a traumatic injury. The vegetative form of the noninvasive organism releases powerful exotoxins that circulate and become fixed to CNS, producing the disease. The diagnosis of tetanus is entirely a **clinical diagnosis** and it depends on 4 criteria:

- History of traumatic injury, one to several weeks ago.
- Trismus (inability to open the mouth) is the most characteristic feature.
- Hyperexitability with generalized muscular stiffness and tonic spasms.
- Complete alertness with no evidence of altered consciousness.

Urgent management of tetanus includes the following aspects:

1. Neutralization of circulating toxins by antitetanic serum: A skin sensitivity test is made first to exclude hypersensitivity and then 50.000 units are given I.V. and another 50.000 units are given I.M. The value of the antitetanic serum is to prevent further fixation of toxins but it has no effect on the already fixed toxins that will be metabolized by the body within 2 - 6 weeks. If **human tetanus immune globulin** ***(Tetuman vial, 250 unit/2 ml)*** is available, it should be given intramuscular in a dose of 3000 - 6000 unit. It is preferable than antitetanic serum as its administration is not followed by allergy or anaphylaxis.

2. Eradication of the vegetative organisms by antibiotics: Crystalline penicillin is given I.V. in a dose of 200.000 unit/kg/day, divided into 4 doses. Duration of therapy is 10 days.

3. Control of hyperexitability, rigidity and tonic spasms: Quiet and environment avoidance of visual and auditory stimuli are important. Sedatives and muscle relaxants in big doses are always required. **Diazepam** is given initially I.V. in a dose of 0.2 mg/kg every 3-6 hours. If the response is inadequate, the dose can be increased to 0.5 mg/kg and **phenobarbital** may be added in a dose of 3 mg/kg, I.V. every 6-8 hours. In extremely severe cases, diazepam or midazolam continuous infusion can be used. Once the condition becomes stabilized and oral intake is possible, treatment can be continued with oral phenobarbital (5 mg/kg/day, in 2 - 3 divided doses). Dosage can be increased if the response is inadequate. Treatment with sedatives and muscle relaxants is usually needed for 2 - 4 weeks. (See sedatives and anticonvulsants).

4. Care of the airway and respiration: Airway obstruction due to severe laryngospasm or aspiration is usually the cause of death. Close observation is essential and equipment for suctioning, endotracheal intubation and mechanical ventilation should be available. In newborns with laryngospasm and respiratory depression, endotracheal intubation and mechanical ventilation should be considered.

5. Care of the umbilicus or the wound: Local cleaning of the umbilicus (in newborns with tetanus neonatorum) or the wound in children is important. Foreign bodies should be removed and the wound is left open because the tetanic organism is anaerobic and wound coverage will help multiplication.

6. Care of feeding: Initial maintenance I.V. fluid therapy is usually required during the first few days until an adequate control of the muscular stiffness and tonic spasms is achieved. If oral intake is not possible because of the severe trismus, nasogastric tube feeding should be made. In older children not tolerating tube feeding, gastrostomy may be necessary (see nutrition, tube feeding). Once oral intake is possible it should be resumed gradually.

Mortality rate is above 50%. It is higher in neonates and in those with short incubation period or with severe disease. Certainly, proper management and good nursing care can significantly improve the outcome.

Practical example

A newborn, 7 days old (3 kg) with tetanus neonatorum.

Hospitalization (in quiet room)

+ *Close observation.*
+ *I.V. fluid therapy:* — Kadalex: 360 ml — Saline: 90 ml | over 24 hours (6 drops/minute).

  (To be repeated on the second day and then gradually replaced by nasogastric tube feeding).
+ *Antitetanic serum:* 50.000 units I.V. and 50.000 units I.M.
+ *Antibiotic therapy:* Crystalline penicillin 150.000 units, I.V. every 6 hours for 10 days.
+ *Anticonvulsant:* Phenobarbital: 15 mg I.V., then 10 mg I.V. every 8 hours for 2 - 3 days to be replaced with oral preparations.

± *Mechanical ventilation.*

+ *Care of umbilicus.*

5. Diphtheria

Infection with corynebacterium diphtheria usually occurs by contact with a carrier or a patient. Clinical manifestations appear after an incubation period of 1 - 6 days and the severity of illness will depend mainly on the immunological status of the patient and the site of involvement. Nasal, pharyngeal or laryngeal diphtheria should be differentiated from other causes of nasal discharge, tonsillar membrane or stridor, respectively. Clinical diagnosis is confirmed by a **culture** of a material from the membrane. Microscopic examination of the material is unreliable.

Management of diphtheria includes the following aspects:

1. Absolute bed rest: It is extremely important for 2-3 weeks to lessen the incidence of myocarditis. Daily examination of the heart and recording of heart rate is essential. Repeated ECG (every 3 - 4 days) is recommended.

2. Neutralization of circulating toxins by antidiphtheretic serum: A skin sensitivity test is made first to exclude hypersensitivity, then 50.000 - 100.000 unit are given I.V. Adrenaline should be available for the possible allergic reactions.

3. Eradication of the organisms by antibiotics: One of several drugs can be given. Procaine penicillin (400.000 I.U., I.M., once daily) or erythromycin (50 mg/kg/day, oral, in 4 divided doses) or amoxycillin (50 mg/kg/day, oral, in 4 divided doses) are all effective. Duration of therapy is 10 days.

4. Treatment of complications: Myocarditis and bulbar paralysis are the most serious complications. In severe cases, the incidence of myocarditis can be lessened by corticosteroids. Prednisone is given orally in a dose of 1 mg/kg/day is divided doses for 2 weeks. With myocarditis, absolute bed rest is enforced and digitalization may be required if congestive heart failure develops. With bulbar paralysis, tube feeding is indicated to avoid aspiration and may be continued until spontaneous recovery occurs.

5. Vaccination after recovery: The acquired immunity of diphtheria is inadequate, so immunization after recovery is necessary.

6. Health precautions: Close contacts should receive a booster dose of diphtheria toxoid and a course of erythromycin or procaine penicillin for 7 - 10 days.

6. Scarlet Fever

Scarlet fever is a common disease mostly seen in children between the age of 3 - 10 years. The disease is more common during the late winter and spring seasons.

Management of scarlet fever includes the following aspects:

1. Antibiotic therapy: It is important to eradicate the streptococcal infection and to shorten the duration of illness. Oral phenoxymethyl penicillin ***(Ospen suspension, 400.000 unit/5 ml)*** is the drug of choice. It is given in a dose of 50.000 unit/kg/day, in 3 divided doses for 10 days. In patients sensitive to penicillins, erythromycin ***(Erythrocin or Erythrin suspension, 200 mg/5 ml)*** can be used as an alternative in a dose of 50 mg/kg/day, in 3 divided doses, for 10 days. Parents should be oriented with the importance of complete eradication of streptococcal infection and should be instructed to complete the course of 10 days especially in areas where rheumatic fever is common. Recently, new macrolides as clarithromycin ***(Klacid suspension, 250 mg/5 ml)*** or azithromycin ***(Zithromax OR Xithrone suspension, 200 mg/5 ml)*** can be also used. For dosage, see macrolides. First-generation cephalosprins as cephalexin ***(Ceporex or Keflex suspension ,250 mg/ 5 ml)*** can be also used in a dose 50 mg/kg/day, in 3 divided doses, for 7-10 days.

2. Antipyretics: Paracetamol can be used for few days to control the fever and to relieve the sore throat. With antibiotic therapy, these symptoms usually disappear within few days. Other antipyretic drugs may be used as an alternative to paracetamol (for dosage, see antipyretics).

3. Activity and diet: Bed rest is indicated during the first few days where fever, vomiting and abdominal pain are present. After subsidence of these symptoms, each child will determine his own level of activity. During the first few days, liquids and soft diet are more tolerable than other foods.

4. Health precautions: The disease is not highly infectious, so strict isolation is not necessary. It is important for parents to realize that the child becomes noninfectious after 24 hours only of initiation of antibiotic therapy. The child can return to school after 10 days of onset of illness (i.e. with discontinuation of antibiotic therapy).

5. Follow-up: Re-examination after 3 weeks of onset is advisable to exclude the late complications as rheumatic fever or post-streptococcal glomerulonephritis.

7. Measles

With compulsory vaccination programs, measles has become a relatively uncommon disease. However, in vaccinated children, the disease may also occur, but usually in a mild or altered form.

Management of measles includes the following aspects:

1. Symptomatic treatment: Measles is a self-limited disease, and in most cases, all manifestations of illness will disappear over a period of 10 days. During this period, symptomatic treatment is the main line of therapy:

(a) Antipyretics: Paracetamol or ibuprofen can be used during the first week of illness (see antipyretics). The fever usually subsides spontaneously 2 - 3 days after the onset of rash.

(b) Cough medicines: Cough is a constant manifestation of measles so that the diagnosis cannot be made in absence of cough. During the first few days, cough suppressants as pholcodin, dextromethorphan or butamirate may be used to give symptomatic relief. With expectoration these medications are contraindicated and expectorants may be used.

(C) Nose and eye decongestants: Nose drops and eye decongestant drops may be prescribed during the prodromal stage when these manifestations are prominent. Naphazoline drops ***(Prisoline or Nostamine drops)*** can be used for both, eye and nose. Three instillations per day are usually sufficient.

2. Antibiotic therapy: It is only indicated in presence of bacterial complications as otitis media or pneumonia. For otitis media, broad-spectrum penicillin as ampicillin or amoxicillin, given orally, is sufficient but for pneumonia, hospitalization and parenteral antibiotic therapy are indicated.

3. Activity and diet: Best rest for one week in a warm room is important. Adequate fluid intake and soft diet during this week is indicated. The patient should not be forced to eat.

4. Health precautions: Measles is a highly infectious disease. Isolation is recommended from the onset of catarrhal stage and up to 4 days after the onset of rash. However, isolation is usually of little value because the patient is also infectious during the last 5 days of incubation period. Unvaccinated exposed siblings can be protected by passive immunization with gamma globulin injection (1-2 ml, I.M.). Hyper-immune globulin for measles, if available, is preferable ***(Moruman vial)***. If this passive immunization is given within 5 days of exposure, measles can be prevented. If the patient is hospitalized, protection is also indicated for contacts in hospital wards. The child can return to school after 2 - 3 weeks of onset of illness.

8. Chickenpox

Although chickenpox can occur at any age even in neonates, most cases are usually seen between the ages of 2 - 10 years. Chickenpox during this age group usually runs a mild and benign course, but in neonates and young infants the disease may be serious or even fatal.

Management of chickenpox includes the following aspects:

1. Measures to control itching: Itching is the main problem and main annoying complaint of chickenpox.

(a) Antihistamines: Drugs as promethazine ***(Phenergan syrup)*** clemastine ***(Tavegyl syrup)*** or mequitazine ***(Primalan syrup)*** may be used for 5 - 7 days (See antihistamines for dosage).

(b) Local application of soothing agents: Application of a soothing agent as calamine lotion ***(Calamine or Caladryl lotion)*** twice daily may be also useful. It is important to mention that the common mistake of applying the disfiguring gentian violet should be avoided.

(c) Fingernails should be kept cut: This is important to prevent scratching and to avoid secondary bacterial infection.

2. Antipyretics: Paracetamol can be used for few days when fever is present. However, in most cases, fever is mild and needs no therapy.

3. Antibiotics: They are only indicated in secondary bacterial infection. Oral erythromycin (50 mg/kg/day, in 3 divided doses) or a first-generation cephalosporin as cephalexin (50 mg/kg/day, in 3 divided doses) can be used for 5 - 7 days.

4. Health precautions: Chickenpox is a highly infectious disease. The patient is infectious 1 -2 day before the rash and up to 5 - 6 days after onset until all lesions are crusted. Isolation for one week is recommended and the child can return to school after 7 - 10 days. Exposed siblings between the ages of 1 - 10 years need no protective measures, but neonates and young infants should receive passive immunization by I.M. gammaglobulin injection (1 - 2 ml, I.M.). Patients with immunodeficiency or those receiving immunosuppressive drugs should also receive prophylaxis. If a susceptible sibling attracts the disease, the clinical manifestations will appear after an incubation period of 3 weeks.

5. Treatment of complications: Severe varicella pneumonia is treated by I.V. acyclovir (see antiviral drugs). Neurological complications as acute cerebellar ataxia, Guillain Barre Syndrome or facial nerve palsy are managed accordingly.

9. Mumps

Mumps is by far the commonest cause of acute parotid swelling in children. Most cases occur below the age of 15 years. With routine vaccination against mumps, the incidence has markedly decreased, but vaccinated children may also catch the disease. Mumps in vaccinated children is usually milder, not associated with fever and not infectious to susceptible contacts.

Management of mumps is entirely symptomatic:

1. Antipyretics: Paracetamol ***(Pyral or Paramol syrup, 120 mg/5 ml)*** or ibuprofen ***(Brufen or Marcofen syrup, 100 mg/5 ml)*** can be used to relieve fever and local pain of the affected glands. In most cases, fever, if present, will subside over few days and local pain is usually not severe and well tolerated by most children. Local applications over the inflamed glands have no value and should not be done.

2. No antibiotics are needed, as the disease is viral and bacterial complications do not occur.

3. Activity and diet: There is no evidence that bed rest will prevent complications, so activity should be guided by the patient's tolerance. Bed rest is only indicated in presence of complications as meningoencephalitis, pancreatitis or orchitis. The diet should be adjusted according to the patient's ability to chew.

4. Health precautions: The patient is infectious during the last week of incubation period and up to 10 days after onset of parotid swelling. Isolation is recommended until swelling subsides. The child can return to school after 2 weeks of onset. It is important to remember that mumps in vaccinated children is not infectious. If a susceptible unvaccinated sibling attracts the disease, the clinical manifestations will appear after an incubation period of 2-3 weeks.

5. Treatment of complications: Complications are generally unusual in children. Meningoencephalitis, which is the commonest complication, manifests clinically by just moderate neck stiffness and without any other neurological manifestations. Bed rest is indicated and mortality is rare. Pancreatitis is usually mild. Orchitis is unusual in children, but if it occurs, bed rest and local support are sufficient. Arthritis, which is rare, may necessitate corticosteroid therapy for 2 weeks.

4

Neurology

1. Febrile Convulsions.
2. Epilepsy.
3. Comatose Child.
4. CNS Infections.
5. Poliomyelitis.
6. Infective Polyneuritis.
7. Rheumatic Chorea.
8. Mental Retardation.

1. Febrile Convulsions

Febrile convulsions is a common clinical problem in pediatric practice. Clinical diagnosis depends on 5 clinical criteria. Exclusion of CNS infections is the most important clinical problem (see Pediatric Clinical Diagnosis).
Management of febrile convulsions includes the following aspects:

1. Control of the convulsive fit: As the convulsive fit in febrile convulsions is usually short (5-10 minutes), the convulsions usually cease before the patient arrives to the hospital, and because the post-ictal stupor is also short, the patient almost regains the normal alertness at time of examination. However, occasionally, the patient may be still convulsing at the time of examination. In this case, **diazepam** ***(Neuril OR Valpam amp, 10 mg/2 ml)*** is given I.V. in a dose of 0.5 mg/kg. If convulsions cease during injection, don't complete the calculated dose. When an I.V. line cannot be established, the calculated dose can be given rectally by a syringe and flexible tube or diazepam rectal tubes can be used ***(Diazepam or Stesolid rectal tubes, 5 mg).*** As a second convulsive fit during the same illness is very rare, a maintenance dose of anticonvulsant is not necessary. However, observation for 24 hours in a hospital may be indicated especially with very anxious parents. If convulsions recur, lumbar puncture and CSF examination is indicated to exclude CNS infections.

2. Control of the high fever: Tepid sponges and baths are needed to lower the body temperature. Paracetamol (oral or rectal) is also given. In case of hyperpyrexia (temperature above 41.0°C), I.V. acetylsalicylic acid ***(Aspegic injectable)*** is given in a dose of 10-15 mg/kg. Paracetamol is then prescribed every 6 hours for 1 - 2 days to prevent further elevation (See antipyretics).

3. Control of the extracranial infection: With focal infections as tonsillitis or otitis media, a specific oral antibiotic is prescribed according to the clinical diagnosis. In case of simple fever, an oral broad- spectrum antibiotic as amoxycillin for 5 days seems reasonable.

4. Prevention of recurrence in subsequent febrile illnesses: Parents should be oriented that convulsions may recur with subsequent febrile illnesses. Measures to lower the temperature at the onset of any febrile illness are important. Fortunately, in more than 50% of cases, convulsions will not recur, and in another 30% of cases, it recurs once or twice. In case of recurrence, oral **diazepam** ***(Valium OR Valpam syrup, 2 mg/5 ml)*** is recommended during the febrile episodes in a dose of 1 mg/kg/day, in 3 divided doses, for 2-3 days. In case of frequent recurrences (3-4 fits/year), EEG is indicated and a prophylactic antiepileptic therapy with **sodium valproate** ***(Convulex drops, 10 mg/drop)*** can be used in a dose of 10-20 mg/kg/day, for one year following the last fit. Other antiepileptics as phynetoin and carbamazepine are not effective.

2. Epilepsy

Management of epilepsy aims to control the ongoing convulsive fit by I.V. drugs and to prevent recurrence by chronic use of oral drugs.

A) Management of the ongoing convulsive fit

1. Patent airway: Insert an oral airway and suction the oropharynx. It is better to keep the patient on his side to minimize the possibility of aspiration.

2. Oxygen therapy: It is important to preserve brain functions and to avoid brain anoxia. A concentration of 40-60% with a facemask is sufficient.

3. Immediate I.V. line: It is very essential to provide the infusion of glucose 10 % (5 ml/kg) and to give the anticonvulsant drugs. Initial blood sample for investigations should be withdrawn.

4. Immediate I.V. anticonvulsants: Beyond the neonatal period, **diazepam** is the drug of choice. It is given in a dose of 0.5 mg/kg over 3 minutes. If convulsions cease during injection, don't complete the calculated dose. If it is not effective within 10 minutes, **phenobarbital** is given I.V. in a dose of 15-20 mg/kg over 3 minutes. If convulsions continue for another 10 minutes, **phenytoin** is given in a dose of 15-20 mg/kg over 5 minutes. Following the initial control, a maintenance dose of phenobarbital (2 -3 mg/kg, I.V., every 8 -12 hours) and/or phenytoin (2 -3 mg/kg, I.V., every 8 -12 hours) may be needed for a day or two to prevent recurrence.

5. Management of refractory cases: With failure of the above 3 drugs, the patient should be transferred to ICU where a more aggressive measures should be taken:

(a) Diazepam constant infusion (0.2 mg/kg/hour) can be initially tried. Practically, 2 ml diazepam (10 mg) is added to 100 ml saline or Ringer's lactate (1 mg/10 ml) and the infusion is made at a rate of 2 ml/kg/hour. The dose can be adjusted according to the response and the side effects.

(b) Midazolam constant infusion (0.1 mg/kg/hour) can be tried when diazepam infusion is not effective. Practically, 1 ml midazolam (5 mg) is added to 100 ml saline or Ringer's lactate (1mg/20 ml) and the infusion is made at a rate of 2 ml/kg/hour.

(c) Alternative anticonvulsants are the last resort after failure of the above 2 measures. One of 3 drugs can be then tried: **Paraldehyde** (150-200 mg/kg/dose), **lidocaine** (1-2 mg/kg/dose) or **pentobarbital** (2-4 mg/kg/ dose). Initial control with any of these drugs should be followed by a constant infusion for several hours. These serious drugs should be only used in ICU.

B) Prevention of recurrence by oral drugs

When the patient is coming with a history of recurrent convulsions, chronic use of oral antiepileptic drugs is necessary until the convulsions become unlikely to recur. The following rules are important for the long-term therapy:

1. Accurate diagnosis: Diagnosis of the cause of epilepsy can be achieved by both clinical and laboratory studies. Electroencephalogram (EEG) is initially made to confirm the presence of an epileptic focus and to diagnose the type. ***Deficiency states*** as hypoglycemia, hypocalcemia and hypomagnesemia should be routinely excluded in every case and before considering the condition as idiopathic epilepsy. Unfortunately, many patients with these deficiency states were wrongly treated, for several years, as idiopathic epilepsy.

2. Choice of drugs: The 6 main oral antiepileptic drugs are:

- Phenobarbital: 3 - 8 mg/kg/day.
- Phenytoin: 5 - 8 mg/kg/day.
- Carbamazepine: 10 - 20 mg/kg/day.
- Sodium valproate: 20 - 30 mg/kg/day.
- Clonazepam: 0.1 - 0.2 mg/kg/day.
- Ethosuximide: 20 - 30 mg/kg/day.

The daily dose is divided into 2 - 3 doses. (see antiepileptic drugs).

Recent 4 antiepileptic drugs (lamotrigine, gabapentin, topiramate, vigabatrin) may be also used in certain conditions (see antiepileptic drugs). The choice of the appropriate drug depends on the type of epilepsy and the age of the patient.

(a) Grand mal (tonic-clonic) epilepsy: Two drugs (carbamazepine + sodium valproate) are currently the most commonly used drugs. Phenobarbital has become less popular because of the high incidence of behavioural changes and depression of cognitive functions. Phenytoin has several side effects.

(b) Petit mal epilepsy: Sodium valproate or clonazepam can be initially tried. Ethosuximide is also effective.

(b) Myoclonic epilepsy: Partial response may occur with sodium valproate or clonazepam (both drugs should not be used together, see below). The treatment of choice is prednisone or prednisolone (2 mg/kg/day, oral in divided doses) for several weeks. After initial response, the dose can be gradually tapered. Alternatively, ACTH (40 - 80 I.U/day) can be used for several weeks.

3. Number of drugs: Treatment usually starts with **one drug** and at low dosage. The dose is gradually increased, every few days, until seizures are controlled or the maximum dose is reached. It is important to remember that an effective therapeutic blood level is not attained before 4 - 7 days of initiation of therapy, so dosage should not be increased except after the first week. A **second drug** is only added after failure of the first drug, at high dosage, to control the condition. Combination of clonazepam and sodium valproate is contraindicated as it may lead to petit mal status.

4. Monitoring of response: There are individual variations in response to antiepileptic drugs, so dosage should be adjusted according to the response. In cases difficult to control and when the maximum dose is approached, estimation of the serum concentration of the used drug or drugs is useful. Therapeutic serum concentration of the main drugs is:

- Carbamazepine: 5-10 mg/liter.
- Sodium valproate: 50-100 mg/liter.
- Clonazepam: 0.01 - 0.02 mg/liter.
- Phenobarbital: 10-30 mg/liter.
- Phenytoin: 10-20 mg/liter.

5. Duration of therapy: Antiepileptics are continued for 2-3 years after the last seizure and then gradually withdrawn over a period of 6 month.

6. Orientation of parents: Parents should know the possible side effects and the early signs of toxicity of the used drug or drugs:

- Drowsiness is common with most of them, especially with onset of therapy.
- Drug rash: It may occur with phenobarbital or phenytoin.
- Hair changes: Hirsutism with phenytoin and alopecia with sodium valproate.
- Blood disorders and liver dysfunction: Although these complications are rare, periodic evaluation of liver functions and blood elements seems reasonable.

Practical examples

1. A child, 3 years old (15 kg) with idiopathic grand mal epilepsy.

RI Depakine syrup (200 mg/ml) OR Convulex drops (10 mg/drop).
150 mg, oral, every 12 hours.

OR RI Sominaletta syrup (15 mg/5 ml) or Sominaletta tablets (15 mg).
One teaspoon (5 ml) or one tablet, 3 times daily
or one and half teaspoon or one and half tablet, every 12 hours.

2. A child, 6 years old (20 kg) with idiopathic grand mal epilepsy.

RI Tegretol suspension (100 mg/5 ml).
One teaspoon (5 ml), every 12 hours.

OR RI Epanutin suspension (30 mg/5 ml).
Two teaspoons (10 ml), every 12 hours.

3. A child, 3 years old (15 kg) with petit mal epilepsy.

RI Depakine syrup (200 mg/ml) OR Convulex drops (10 mg/drop).
150 mg, oral, every 12 hours.

OR RI Zarontin syrup (250 mg/5 ml).
Half teaspoon (2.5 ml), 3 times daily.

4. An infant, 9 months old (10 kg) with myoclonic epilepsy.

RI Rivotril drops (0.1 mg/drop).
5 drops, oral, every 12 hours.

3. Comatose Child

Coma is a serious, potentially fatal, neurological emergency. Urgent measures are always needed to reach the diagnosis and to provide the necessary therapeutic lines.

Management of a comatose patient includes the following aspects:

A) Clinical evaluation

Simultaneous history and physical examination should be directed to assess the following aspects:

- Level of consciousness.
- Level of dysfunction.
- Associated neurological findings.
- Associated clinical findings.
- The cause.

(For details, see Pediatric Clinical Diagnosis).

B) Laboratory investigations

When the clinical diagnosis is uncertain or the examination fails to suggest a specific cause, laboratory investigations become necessary.

- **Main investigations** include:

- Blood sugar level.
- Blood urea and creatinine.
- Serum electrolytes (Na, K, Ca and Mg).
- Blood gas analysis (pH, HCO_3 and $PaCO_2$).
- Serum transaminases (SGOT and SGPT) and blood ammonia level.
- Complete blood count (CBC) and C-reactive protein (CRP).
- Lumbar puncture and CSF examination.

- **Other investigations** may be also needed according to the clinical situation. CT scan of the head is indicated in case of head trauma or in presence of focal neurological signs. Coagulation studies are needed in those with suspected bleeding disorders as hemophilia or DIC. Analysis of gastric contents is important when the possibility of poisoning is considered.

C) Nonspecific management

The comatose patient should never be left unattended and he should be admitted to ICU unit. Nonspecific management aims to preserve brain functions, to provide nutritional support and to treat the complications. Management should always start with the ABC (Airway + Breathing + Circulation).

1. A: Airway: Measures to keep the airway patent are the initial step. The mouth is opened and any food remnants or foreign bodies should be removed. Suctioning of the oropharynx is made, the neck is slightly extended and an oral airway is inserted.

2. B: Breathing: All comatose patients should receive oxygen. An initial concentration of 40%, given by a head box (in infants) or facemask or nasal catheter (in children), is usually sufficient. Oxygen therapy should continue until the patient regains consciousness. Severe respiratory depression with CO_2 retention necessitates mechanical ventilation.

3. C: Circulation: Following patent airway and oxygen administration, an I.V. line should be immediately inserted. Blood pressure should be kept within normal limits and shock (hypotension) or hypertension, if present, should be promptly corrected. When the possibility of diabetic ketoacidosis is standing, start therapy with Ringer's lactate or normal saline (see diabetes). Otherwise, I.V. fluid therapy is made of glucose 10% and saline in a ratio of 4:1 in an amount equal to the daily maintenance requirements. When renal failure is excluded, potassium chloride solution should be added. Dehydration and/or electrolyte disturbances should be also corrected (see I.V. fluid therapy). An accurate fluid balance of intake and output should be made. Daily weighing is essential.

4. Control and prevention of convulsions: If convulsions are present, vigorous therapy to control the convulsions and to prevent further fits is essential. **Diazepam** is given I.V. in a dose of 0.5 mg/kg to control the ongoing convulsive fit. If it is not effective within 10 minutes, **phenobarbital** is given I.V. in a dose of 15 mg/kg. Continued convulsions for another 10 minutes necessitates I.V. **phenytoin** in a dose of 15 mg/kg. Following the initial control, a maintenance therapy is made with I.V. phenobarbital (2 -3 mg/kg every 8 -12 hours) and/or phenytoin (2 -3 mg/kg every 8 -12 hours). Treatment is continued until convulsions become unlikely to occur then the drugs are gradually discontinued (See anticonvulsants and epilepsy).

5. Control of the increased intracranial pressure: Increased ICP is suspected by increased muscle tone, hyper-reflexia and sluggish pupillary reaction to light. Unilaterally dilated irreactive pupil is a sign of uncal herniation, which necessitates immediate mechanical hyperventilation. CT scanning of the head may be done to demonstrate the brain oedema. Management includes:

(a) Elevate the head 30° (in neutral position) to enhance cerebral venous return.

(b) Decrease I.V. fluids to 60 - 70% of daily requirements.

(c) Use dehydrating measures: Give dexamethasone (0.25 mg/kg, I.V. every 6 - 12 hours). Mannitol 20% (5 - 10 ml/kg, I.V. over 30 minutes, every 6 hours) may be also used. Furosemide (2 mg/kg I.V. every 12 hours) may be added in severe cases. If these drugs are not effective within 2 days, they should be discontinued. Care should be taken to avoid volume overload with mannitol therapy.

(d) In severe cases and when all above measures are ineffective, mechanical ventilation is used to induce hyperventilation to keep $PaCO_2$ just below 30 mm Hg. CO_2 wash is useful to decrease the cerebral blood flow.

6. Care of the respiratory system: Prophylactic chest physiotherapy and frequent suctioning are important to prevent lung collapse. A nasogastric tube is inserted and gastric contents are aspirated to avoid vomiting and possible inhalation. Apart from anticonvulsants, all drugs that may suppress the respiration should be avoided. Complications as pulmonary infection or pulmonary oedema should be treated. Severe respiratory depression with CO_2 retention ($PaCO_2$ above 60 mmHg) necessitates mechanical ventilation.

7. Care of the gastrointestinal system: Stress gastric ulceration is common in comatose patients. An antacid as aluminium hydroxide gel ***(Epicogel or Alkagel suspension)*** is given through the nasogastric tube every 4 hours in an amount of 10 -15 ml/time. Prevention of constipation and fecal impaction is also important. Lactulose ***(Lactulax or Laxolac syrup)*** may be used through a nasogastric tube to prevent or treat constipation (See laxatives).

8. Care of the eyes and skin: Antibiotic eye drops and ointment are used to prevent infection and corneal ulcerations. Frequent change of position is important to avoid bedsores. A urine bag is placed to collect urine and to avoid contact with the skin. Fecal matters should be immediately removed and proper care of the napkin area is important. Skin infections should be adequately managed by both local and systemic measures.

9. Prevention of infection: Frequent inspection of the I.V. sites is important. Repeated urine analysis and urine and blood cultures are indicated in prolonged coma. A prophylactic broad-spectrum antibiotic may be used I.V. when the risk is considerable.

10. Nutritional support: When coma persists for more than 2 - 3 days, nasogastric tube feeding should be started to provide the nutritional requirements. Don't forget that tube feeding was originally designed for comatose patients (see tube feeding). When tube feeding is not tolerated, total parenteral nutrition should be considered.

D) Specific management

Treatment of the underlying cause of coma is an essential step in management. The cause could be known by a collection of data gained by detailed history, thorough examination and relevant investigations.

1. Intracranial infections: Until a bacterial origin is excluded, all patients with CNS infection (meningitis, encephalitis, or brain abscess) should receive vigorous I.V. antibiotic therapy. An initial therapy with ampicillin (200 mg/kg/day, in 4 divided doses) and one of the third-generation cephalosporins as cefotaxime (200 mg/kg/day, in 2 divided doses) is recommended. In bacterial

meningitis, antibiotic therapy may be changed according to the clinical response and results of CSF and blood cultures, duration of therapy is at least for 10 - 14 days. In brain abscess, urgent surgical consultation and surgical drainage is important and antibiotic therapy is continued for 6 weeks. In encephalitis due to herpes simplex infection, acyclovir ***(Zovirax)*** should be used I.V. (see antiviral drugs).

2. Head trauma and intracranial hemorrhage: Initial CT scan of the head is essential. Urgent neurosurgical consultation and possible surgical intervention are indicated.

3. Hypoxic encephalopathy: In case of severe hypoxia due to severe respiratory failure, mechanical ventilation is necessary. Severe cardiogenic or septic shock requires inotropic therapy with dopamine and/or dobutamine infusion. Severe acute anemia should be urgently corrected by packed red cell transfusion (5-10 ml/kg).

4. Endogenous encephalopathy: Diabetic coma requires parenteral insulin therapy (see diabetes). In hepatic or renal coma, several specific measures are required (see acute hepatic failure and acute renal failure). Hyponatremic dehydration requires specific therapy with I.V. fluids and hypertonic saline infusion (see I.V. fluid therapy).

5. Exogenous encephalopathy (Drug intoxication): In case of accidental poisoning (with a medicine, cleaning agent, insecticide, paints, petroleum product or a plant), several general rules should be followed:

(a) Supportive measures: Treatment of any failing system or systems is the most important item in management. Respiratory, cardiovascular and neurologic support should always come first. It is not very important to know the responsible drug or poison but what is more important is to detect and correct the adverse effects of that drug (See Pediatric Critical Care).

(b) Decrease absorption of the toxin: Emptying the stomach through gastric lavage is useful in removing the remaining toxin in the stomach.

(c) Increase excretion of the toxin: This is done by forced diuresis. Give furosemide and mannitol I.V. and increase I.V. fluids to 1.5 the maintenance.

(d) Poison identification: By history, taking sample of the agent and the container, taking samples of blood, urine and vomitus to be sent for toxicology center.

(e) Give specific antidote (if available): Atropine should be always in mind as antidote for organic phosphate poisoning. Pinpoint pupils are the most important clinical finding. Consultation of a poisoning center is important.

4. CNS Infections

Once the diagnosis of CNS infection is made or even suspected, **hospitalization** is necessary for close observation, urgent investigations and immediate management. **Initial investigations should include:**

- CSF examination: Cautious lumbar puncture is made with a narrow needle and while the patient is lying on his side to avoid medullary herniation. CSF examination should include cultures for bacteria. A second examination should be made after 24 - 48 hours to evaluate the response to therapy and a third one is made at the end of therapy.
- Complete blood count (CBC), C-reactive protein (CRP) and blood culture.
- When brain abscess is suspected, CT scan of the head is indicated.
- In suspected tuberculous meningitis, tuberculin test, chest x-ray and examination of gastric contents for acid-fast bacilli are important.

Management of CNS infections includes the following aspects:

1. Antibiotic therapy: Until a bacterial origin is excluded, all patients with CNS infection (meningitis, encephalitis or brain abscess) should receive vigorous I.V. antibiotic therapy. A **third-generation cephalosporin** as cefotaxime (200 mg/kg/day), cefoperazone (200 mg/kg/day), ceftriaxone (100 mg/kg/day) or ceftazidime (100 mg/kg/day) is currently considered as the initial treatment of choice. **Ampicillin** (200 mg/kg/day) may be also added. The use of **chloramphenicol** in bacterial meningitis (100 mg/kg/day) should be limited to patients who are sensitive to cephalosporins. Duration of therapy in bacterial meningitis is 10 - 14 days or at least for 5 days after the patient becomes afebrile. In case of brain abscess, antibiotic therapy should be continued for 6 weeks and neurosurgical consultation and possible drainage are important. In tuberculous meningitis, triple drug therapy with isoniazid, rifampicin and pyrazinamide is indicated in conjunction with corticosteroid therapy (see antituberculous drugs). In patients with encephalitis due to herpes simplex infection, antiviral therapy with I.V. acyclovir is indicated (see antiviral drugs).

2. I.V. fluid therapy: It is usually needed during the first few days because of the risk of vomiting and aspiration. The solution used should be made of glucose 10% and saline in a ratio of 4: 1 with addition of potassium chloride solution 15% (1 ml for each 100 ml solution). The amount given per day should only equal 70% of the maintenance because of the commonly associated inappropriate secretion of antidiuretic hormone and also to minimize brain oedema. Oral intake should be resumed as soon as the condition allows. If the patient is still comatose after 2 -3 days of onset, nasogastric tube feeding should be started (see tube feeding).

3. Control and prevention of convulsions: Vigorous therapy to control the ongoing convulsive fit and to prevent further fits is important. **Diazepam** is given I.V. in a dose of 0.5 mg/kg to control the convulsive fit. If it is not effective within 10 minutes, **phenobarbital** is given I.V. in a dose of 15 mg/kg. Continued convulsions for another 10 minutes necessitates I.V. **phenytoin** in a dose of 15 mg/kg. Following the initial control, a maintenance therapy is made with phenobarbital (2 -3 mg/kg, every 8 -12 hours) and/or phenytoin (2-3 mg/kg, every 8 -12 hours). Treatment is continued until convulsions become unlikely to recur then the drugs are gradually discontinued.

4. Care of comatose patient: In case of coma, all measures mentioned under the nonspecific management of coma should be followed.

5. Health precautions: Patients with bacterial meningitis are not infectious after 24 hours of initiation of antibiotic therapy and can be removed from isolation and managed in ordinary wards. In contrary to what is thought by many people, CNS infections are not highly infectious. In close contacts, the possibility of being infected (infectivity rate) is not more than 1%. Health precautions are not necessary for hospital personnel. For close family contacts, prophylaxis with rifampicin (20 mg/kg/day, in 2 divided doses for 3 -5 days) is recommended in documented meningococcal meningitis. Total daily dose should not exceed 600 mg.

6. Follow-up after recovery: In case of recovery, several neurological sequelae may occur, and a periodic follow up is essential. Mental retardation, organic epilepsy and motor weakness may occur. Regular periodic measurement of head circumference in recovered infant is important to exclude postmeningitic hydrocephalus and chronic subdural effusion.

Practical example

An infant, 10 months old (10 kg) with bacterial meningitis.

Hospitalization

+ ***Isolation (for 24 hours only)***
+ ***I.V. fluid therapy***: - Glucose10%: 600 ml
  - Saline: 150 ml
  - KCl 15%: 7.5 ml

  over 24 hours (10 drops/minute)

  (To be repeated on the second day and then gradually replaced by nasogastric tube feeding or oral feeding).
+ ***Antibiotic therapy*** - Cefotaxime: 1.0 gm ... I.V. ... every 12 hours.
  - Ampicillin: 500 mg ... I.V. ... every 6 hours.

  (Duration of therapy is 10 - 14 days).
+ ***Anticonvulsants***

± ***Care of comatose patient***

+ ***Repeat C.S.F. examination*** after 48 hours and at the end of therapy.

5. Poliomyelitis

In spite of the compulsory vaccination programs, poliomyelitis is still occasionally encountered in underdeveloped countries. Paralysis usually occurs in unvaccinated or partially vaccinated infants between the age of 3 months and 2 years. The illness runs through 3 stages; the acute stage, stage of restoration and stage of residuals.

A) The acute stage

Acute stage is the first 2 weeks following the onset of paralysis. It can be called **"the stage of pediatrician"**. Medical management during this stage includes the following aspects:

1. Isolation: As the patient is infectious during this stage, isolation especially from susceptible infants is important.

2. Observation: As paralysis may extend to involve other areas, observation is important especially for 2 areas:

- Involvement of muscles of respiration (diaphragm and/or intercostal muscles). Evaluation of the degree of involvement is important and blood gas analysis is essential to exclude central respiratory failure. In case of hypoxemia and CO_2 retention, mechanical ventilation is life saving.
- Involvement of bulbar muscles. In this case, regurgitation and aspiration become a real risk. Nasogastric tube feeding is indicated to avoid aspiration pneumonia. In case of pneumonia, vigorous I.V. antibiotic therapy is indicated.

3. Rest of the paralyzed limbs: The limbs should be kept in neutral position, by using sand bags or other measures, for the first week of illness. Intramuscular injections are absolutely contraindicated during this stage as they may precipitate further paralysis. Passive movements of limbs are gradually allowed during the second week.

B) Stage of restoration

It starts from 2 weeks and up to 6 months. During this stage, gradual incomplete restoration of the muscle power occurs. This stage can be called **"the stage of physiotherapist"**. Physiotherapy, 2 -3 times per week is essential to prevent wasting and deformities.

C) Stage of residuals

After 6 months of onset, further improvement of motor power is not expected. This stage can be called **"the stage of orthopedic surgeon".** Correction of the residual shortening and/or deformities is the main line of therapy.

6. Infectious Polyneuritis

Infectious polyneuritis **(Guillain Barre syndrome)** is the most common cause of acute paralysis in children. Although it is uncommon in infants, it may occur and needs to be differentiated from poliomyelitis as both conditions may cause paralysis of respiratory muscles and bulbar muscles. Such differentiation is particularly important from the prognostic point of view. In poliomyelitis, the recovery is incomplete and residual motor weakness and/or deformities are always present, while in infectious polyneuritis complete recovery over several weeks or months is the rule (see Pediatric Clinical Diagnosis).

The diagnosis of infectious polyneuritis (Guillain Barre syndrome) is mainly a clinical one. Confirmation of the diagnosis is made by the demonstration the elevated C.S.F. proteins. This finding usually appears 1-2 weeks after onset and usually remains for several weeks or months.

Management of infectious polyneuritis includes the following aspects:

1. No isolation: The disease is not directly caused by the infectious agent, but it represents an altered immune response. The lymphocytes become sensitized to myelin proteins and then migrate to peripheral nerves and cause myelin breakdown.

2. Observation: As in case of poliomyelitis, observation for involvement of respiratory muscles and/or bulbar muscles is essential. With central respiratory failure, endotracheal intubation and mechanical ventilation for several weeks may be necessary. With bulbar paralysis, nasogastric tube feeding may be required.

3. Corticosteroids: It is believed that they are useful in severe or prolonged cases. If used, prednisone is given orally in a dose of 1 - 2 mg/kg/day. When a prolonged use is considered, the alternate-day therapy should be made.

4. Intravenous immunoglobulins (IVIG): It is recommended in severe cases with rapidly progressive ascending paralysis especially when accompanied with respiratory involvement. The dose is 300 mg/kg (10 ml/kg), I.V. infusion over 6 - 8 hours, daily for 4 - 5 days (see passive immunization). Recently, combined administration of IVIG and interferon is effective in some patients.

5. Plasmapheresis: It is recently recommended in severe cases especially when accompanied with respiratory involvement. Five cessions are usually needed with 2 days interval between each 2 cessions. Clinical improvement may be evident within days.

6. Physiotherapy: Following the acute stage and during the recovery period, physiotherapy may be useful in preserving muscle bulk and in prevention of deformities. The necessity for and duration of physiotherapy will vary from patient to patient.

7. Rheumatic Chorea

It is the most common form of acquired chorea in childhood. In one third of cases, associated rheumatic heart disease is present. The diagnosis depends on the characteristic clinical findings. The evidence of preceding streptococcal infection is commonly lacking and throat culture or antistreptococcal antibodies are frequently negative (See Pediatric Clinical Diagnosis).

Management of rheumatic chorea includes the following aspects:

1. Reassurance: Parents and the child should be reassured that the condition is transient and it will subside completely over several weeks or few months. Parents should also realize that symptoms may increase in severity during the first few weeks, but this should not create any additional concern.

2. Drug therapy: Sedatives are usually required to allay the nervousness and to prevent the outbreaks of crying. Some improvement of the involuntary movements may be also achieved. **Haloperidol** ***(Safinace drops, 0.1 mg/drop or Safinace tablets, 1.5 mg)*** is recently considered the drug of choice. It is given in a dose of 0.1 - 0.2 mg/kg/day, oral, in 2 divided doses. If the drug is not available, other drugs as **chlorpromazine** ***(Neurazine drops, 2 mg/drop)*** can be used. It is given in a dose of 1 - 2 mg/kg/day, oral, in 3 - 4 divided doses. **Phenobarbital** ***(Sominaletta tablets, 15 mg)*** can be also used, as an alternative, in a dose of 3 mg/kg/day, oral, in 2 divided doses.

3. If associated with active carditis, bed rest and corticosteroids are indicated.

Practical example

A child, 8 years old (26 kg) with isolated rheumatic chorea.

RI Safinace tablets (1.5 mg)
One tablet, oral, twice daily (It is better to start with a half tablet, twice daily, for the first few days).

8. Mental Retardation

Mental retardation is the most handicapping disorder in pediatric practice. The best strategy for dealing with the problem is through prevention. Once the retardation has developed, the management is mainly supportive and aims to normalize the life of the family and the child as much as possible.

A) Prevention of mental retardation

Pediatricians can often play a great role in this respect. The process of prevention can be summarized in 3 basic successive concepts:

1. Prevention of delivery of retarded children: In untreatable inherited disorders, providing a precise genetic counseling to parents could avoid further pregnancies, especially when the risk is great. In case of pregnancy, prenatal diagnosis and abortion of affected fetus are also helpful.

2. Early diagnosis of treatable conditions: The most important treatable conditions are congenital hypothyroidism, galactosemia and phenylketonuria. In developed countries, simple screening tests for detection of these conditions are made for every newborn. These tests are:

- Congenital hypothyroidism: Plain x-ray on knee region or T_3 and T_4 levels.
- Galactosemia: Reducing substance in urine.
- Phenylketonuria: Ferric chloride test (2 drops of ferric chloride solution 2% + 1 ml urine). Green colour suggests phenylketonuria.

In early infancy, any clinical suspicion is an indication for screening tests.

3. Avoidance of situations that lead to acquired retardation: Physicians should be fully aware of illnesses that may lead to brain damage:

- In the immediate postnatal period, anoxia and cyanosis may lead to retardation. Every effort should be made to prevent and correct postnatal anoxia.
- In case of CNS infections, early diagnosis and vigorous adequate antibiotic therapy can significantly reduce the incidence of sequelae.
- In comatose patients, early diagnosis and urgent intervention are crucial. Preservation of cerebral functions by oxygen therapy and glucose is essential.
- Proper control of epilepsy and avoidance of prolonged fits.

B) Management of mental retardation

In lucky situations of making an early diagnosis of a treatable condition, providing the specific therapy will prevent further impairment of mental abilities. Congenital hypothyroidism requires a lifelong therapy with thyroid hormone. In galactosemia and phenylketonuria, treatment is dietary by eliminating the offending substance. i.e. galactose-free milk in galactosemia and phenylalanine-free milk in phenylketonuria (see infant foods).

Otherwise, management of untreatable conditions is supportive and directed for both, parents and the child:

1. Care of parents: the most disastrous event to parents is to get a retarded child. The psychological, social and economic burdens upon the family require real and continuous support. The main aspects of care are:

(a) Telling the diagnosis: Parents usually show anger and do not forgive the physician who firstly made the diagnosis. Wise physicians advise to wait tell the mother discovers by herself that the infant or the child is not developing normally. This attitude may be useful when dealing with untreatable conditions.

(b) Genetic counseling: Parents always ask about possibility of recurrence in further pregnancies. Accurate diagnosis is obviously necessary for providing precise genetic counseling. If the condition is inherited, the recurrence rate should be explained. It is important to remember that in case of trisomy 21, the recurrence rate is not more than 1-2 %, but the risk is higher with mothers above 35 years old. It is very important for the physician to relieve parents from the sense of guilt.

(C) Kind and continuous support and advice: It is very important for the physician to show warm and encouraging attitude. The parent's questions and fears should be dealt with patiently and kindly. Continuous support and advice is probably as important as managing the retarded child.

2. Management of the retarded child: The management aims to normalize the life of the child as much as possible:

(a) Drug therapy: No available magic drug that can regenerate the damaged brain cells. However, some drugs as **pyritinol** ***(Encephabol syrup, 80 mg/5 ml)*** and **piracetam** ***(Nootropil or Stimulan or Neurocet syrup, 200 mg/ml)*** are available in the market and manufacturers unreasonably claim that they are useful. Some physicians use these drugs as psychotherapy for parents who always seek to do something for their child. In children with aggressive behaviour, the use of antipsychotic drugs as **chlorpromazine** is indicated (see psychotropic drugs). Drugs that normalize cerebral blood flow as **vincamine** ***(Oxybral syrup, 10 mg/5 ml)*** may be used to improve intellectual capacity.

(b) Close supervision and constant care: Serious traumas, accidents and accidental poisoning are common in retarded children. The child needs a close supervision and care regarding feeding and other physiological needs.

(c) Stimulation and teaching programs: These programs can be made by parents, specialized centers or institutes. Every retarded child has the right to receive the optimal chance to live as normal as possible.

5

Cardiology

1. Congenital Heart Disease.
2. Acute Rheumatic Fever.
3. Chronic Rheumatic Heart Disease.
4. Infective Endocarditis.
5. Pericarditis.
6. Acute Congestive Heart Failure.
7. Chronic Congestive Heart Failure.

1. Congenital Heart Disease

Management of infants and children with a congenital heart disease requires prior orientation of the type and severity of the lesion as well as the nature and severity of the possible associated complications. Initial clinical, laboratory, radiological and echocardiographic evaluation is essential for planning of successful therapy. Management is generally classified into medical and surgical.

A) Medical treatment

The goal of medical treatment is to maintain the patient's well being and good health as well as to avoid and treat the possible complications.

1. Physical activity: The best guide for physical activity is the patient's own tolerance. Patients with a mild disease need no restriction and they can share in all activities. In moderate to severe heart disease with history of decreased exercise tolerance (exertional dyspnea), some limitation of activity is indicated and competitive sports should be avoided. Fortunately, children with exertional dyspnea will naturally tend to limit their own activity. In patients with chronic congestive heart failure, more restriction of activity is obviously required.

2. Diet: An adequate well balanced diet is important to ensure normal growth and development. In infants with chronic congestive heart failure, feeding difficulties are common and fractionation of feeding into small frequent feeds is important to avoid fatigue and aspiration. Poor milk intake and malnutrition in infancy are indications for early surgical correction.

3.Treatment of possible complications: Patients with congenital heart diseases are susceptible to several complications. Detection and treatment of these complications can significantly improve the outcome of these patients.

(a) Bacterial infections: Patients with plethoric lung fields (as VSD) are liable to recurrent chest infection. These infections may precipitate an episode of acute congestive heart failure. Early diagnosis and vigorous treatment with appropriate antibiotic therapy is important. Prophylactic measures against infective endocarditis are essential during dental procedures or instrumentation of the urinary system. The possibility of infective endocarditis should be considered in every case of unexplained prolonged fever in patients with a congenital heart disease (see infective endocarditis).

(b) Polycythemia: Patients with cyanotic congenital heart diseases should avoid dehydration to prevent the possible thrombotic episodes. Hematocrit value of these patients should be kept between 55-60%. Severe polycythemia with hematocrit value above 65% requires repeated venisection with volume replacement. 5 ml/kg of blood are withdrawn with simultaneous infusion of equal volume of saline or Ringer's lactate.

(c) Iron deficiency anemia: Low or even normal hemoglobin level in patients with cyanotic congenital heart diseases should always raise the possibility of iron deficiency anemia. In proved deficiency, treatment with iron therapy (6 mg/kg/day) will improve the exercise tolerance and will decrease the frequency of paroxysmal hypercyanotic attacks.

(d) Paroxysmal hypercyanotic attacks: These hypoxic spells of increased cyanosis and respiratory distress are peculiar to cyanotic congenital heart diseases with decreased pulmonary blood flow (as Fallot's tetralogy). Short attacks, which last for minutes, are followed by generalized weakness and sleep, while severe attacks may remain for several hours and may progress to unconsciousness and convulsions.

- **Emergency treatment** of severe attacks includes the following:

- Positioning: Calming the infant while held in knee chest position over the mother's shoulder may help to increase the pulmonary blood flow and may abort progression of an early attack.
- Oxygen therapy to correct the hypoxemia.
- Sodium bicarbonate to correct the metabolic acidosis. It is given I.V. in a dose of 2 mEq/kg (4 ml/kg of $NaHCO_3$ 5%) over 10 minutes. The dose can be repeated after 20 minutes if metabolic acidosis persists.
- Propranolol: 0.1 mg/kg, I.V. and may be repeated every 6 hours.

- **Prophylactic treatment** is indicated in severe frequent attacks. Propranolol ***(Inderal tablets, 10 mg)*** is given orally in a dose of 1mg/kg/6 hours. Iron deficiency anemia, if present, should be corrected.

- **Early surgical correction** is indicated in patients with severe frequent attacks.

(e) Congestive heart failure: Patients with a severe congenital heart disease commonly develop chronic congestive heart failure. Manifestations usually appear insidiously over several weeks or months. Feeding difficulties in infants and exercise intolerance in children are early signs. With progression of the condition, dyspnea at rest and manifestations of systemic congestion appear (hepatomegaly and oedema). Treatment with oral digoxin is the main line of therapy. Other drugs as diuretics (furosemide) and afterload reducing agents (captopril) are also used in severe cases. Episodes of acute congestive heart failure are commonly precipitated by respiratory infections and necessitate hospitalization and urgent therapy.

B) Surgical treatment

Surgery is not indicated in every case. Mild asymptomatic lesions require no therapy. The decisions regarding the necessity for surgery and the timing of the operation depends on the nature of the lesion, presence of symptoms and age of the patient.

2. Acute Rheumatic Fever

All patients with acute rheumatic fever should be hospitalized, at least during the first 2 weeks, to allow daily examination. Investigations to prove the inflammatory reactions (CBC, ESR, CRP) and the preceding streptococcal infection (ASO titer) should always be made. Chest X-ray and ECG are essential in presence of carditis.

Management includes the following:

1. Bed rest: It is indicated in all cases. The duration of rest varies with the nature of involvement. In patients with arthritis (without carditis), bed rest for 2 weeks followed by gradual activity for another 2 weeks is sufficient. In those with carditis, bed rest should be for a minimum of 4-6 weeks followed by gradual activity for a similar period.

2. Antimicrobial therapy and prophylaxis: Eradication of any remaining streptococcal infection is made by daily I.M. injection of **procaine penicillin** ***(Penicillin procaine vial or Diacillin vial, 400.000 unit) in*** a dose of 400.000 unit for 10 days followed by a longterm prophylaxis with **benzathine penicillin** ***(Durapen L.A., Lastipen L.A., 1.200.000 unit)*** in a dose of 1.200.000 unit I.M. every 3 - 4 weeks for a minimum of 5 years. In patients with a residual valvular disease (chronic rheumatic heart disease), antimicrobial prophylaxis should be continued up to the age of 20 - 25 years. In patients who cannot tolerate injections, oral **phenoxymethyl penicillin** ***(Ospen suspension, 400.000 unit/5 ml)*** can be used (200.000 unit twice daily).

3. Anti-inflammatory therapy: It is the main line of treatment to suppress the acute manifestations. In case of arthritis (without carditis), **salicylates** ***(Alkasprine or Alexoprine forte tablets, 300mg)*** are given orally in a dose of 100 - 120 mg/kg/day in 3 divided doses, after meals, for the first 2 weeks followed by 75 mg/kg/day for another 4 - 6 weeks. Patients with carditis (with or without arthritis) are treated with oral **prednisone** ***(Hostacorten or Ultracorten tablets, 5 mg)*** in a dose of 2 mg/kg/day in 4 in divided doses for the first 2 weeks followed by gradual withdrawal over the next 2 weeks (decrease the daily dose at a rate of 5 mg every 2 -3 days). When withdrawal begins (after 2 weeks of onset), overlapping therapy with salicylates is given in a dose of 75-90 mg/kg/day and is continued for the next 6 weeks.

4. Treatment of heart failure: In mild to moderate cases, treatment can be made with oral drugs (oral digitalization and oral diuretics). In severe failure, initial parenteral digitalization and diuretics may be indicated. (See congestive heart failure).

Practical examples

1. **A child, 5 years old (18 kg) with acute rheumatic fever. Migratory polyarticular arthritis is present with no evidence of carditis.**

* *Bed rest for 2 weeks followed by gradual activity for another 2 weeks*

RI Penicillin procaine vial OR Diacillin vial (400.000 unit).
One daily I.M. injection for 10 days, followed by:

RI Durapen L.A. OR Lastipen L.A. (1.200.000 unit).
One I.M. injection, every 3 - 4 weeks for a minimum of 5 years.

RI Alkasprine OR Alexoprine forte tablets (300 mg).
Two tablets, 3 times daily after meals for 2 weeks followed by two tablets, twice daily for another 4 weeks.

2. **A child, 6 years old (20 kg) with acute rheumatic fever. Carditis with mild congestive heart failure are evident with no articular manifestations.**

* *Bed rest for 6 weeks followed by gradual activity for another 6 weeks.*

RI Penicillin procaine vial or Diacillin vial (400.000 unit).
One daily I.M. injection for 10 days, followed by:

RI Durapen L.A. OR Lastipen L.A. OR Penadur L.A. (1.200.000 unit).
One I.M. injection, every 3 - 4 weeks, up to the age of 20 years.

RI Hostacorten OR Hostacorten-H tablets (5 mg).
Two tablets, 4 times daily for 2 weeks, then decrease the dose by one tablet every 2 days.

RI Alkasprine OR Alexoprine forte tablets (300 mg).
Starts after 2 weeks of onset of therapy.
Two tablets, 3 times daily, after meals for 6 weeks.

RI Lanoxin Digoxin tablets (0.25 mg).
Two tablets, oral, initially and
One tablet after 8 hours and
Another tablet after another 8 hours, then
Half a tablet, twice daily (every 12 hours).

3. Chronic Rheumatic Heart Disease

Patients with permanent valvular lesions are in need of periodic evaluation. Clinical examination every 1-2 month is important to evaluate the condition and chest x-ray and echocardiography may be needed every 1-2 year for early detection of cardiac enlargement and ventricular hypertrophy.

Management of these patients includes the following aspects:

1. Physical activity: The patient's own ability is the best guide for the range of activity. With history of exercise intolerance, some limitation of physical activity is required. In case of chronic congestive heart failure, more restriction of activity is indicated.

2. Long-term antimicrobial prophylaxis: Benzathine penicillin in a dose of 1.200.000 unit is given I.M. every 3 - 4 weeks up to the age of 20 - 25 years. In patients who cannot tolerate injections, oral phenoxymethyl penicillin ***(Ospen suspension, 400.000 unit/5 ml)*** can be used in a dose of 200.000 unit (half teaspoon) twice daily.

3. Treatment of complications: Patients with chronic rheumatic heart disease are susceptible to several complications. Rheumatic activity, congestive heart failure and infective endocarditis are the main complications.

(a) Rheumatic activity: Rheumatic carditis has the tendency to recur. With every episode of carditis, the patient should be hospitalized and managed as those with acute rheumatic fever.

(b) Congestive heart failure: Manifestations of chronic congestive heart failure can be controlled with chronic oral digoxin therapy. Other drugs as diuretics (furosemide) or afterload reducing agents (Captopril) may be also needed in severe cases. Episodes of acute congestive heart failure precipitated by respiratory infections, rheumatic activity or infective endocarditis may require an initial therapy with parenteral digoxin and furosemide. (See heart failure).

(c) Infective endocarditis: Prophylactic therapy against infective endocarditis is recommended in case of dental procedures or instrumentation. The possibility of infective endocarditis should always be considered in case of prolonged low-grade fever or in those with an episode of acute congestive heart failure (see infective endocarditis).

4. Surgical treatment: It is indicated in those with progressive cardiomegaly or extreme dyspnea with moderate activity. Valvotomy (in stenosis) or valve replacement (in regurgitation) is the standard therapy.

4. Infective Endocarditis

Once the diagnosis of infective endocarditis is suspected, 3 separate blood samples are immediately withdrawn for **blood cultures**. The patient is then **hospitalized** and immediate parenteral antibiotic therapy is started without delay. **Echocardiography** is generally useful to document the presence of vegetations. **Other investigations** as CBC, ESR, C-reactive protein and urine analysis are also useful for follow up.

Management of infective endocarditis includes the following aspects:

1. Bed rest: It is indicated in all cases at least during the first few weeks. In case of heart failure, the duration of rest should extend until recovery.

2. Immediate parenteral antibiotic therapy: When the organism is not yet known, therapy should start with 2 antibiotics:

- Penicillin G: 300.000 unit/kg/day, I.V. (divided into 4 doses, every 6 hours). The dose may be increased up to 20 million/day.
- Gentamicin: 5 - 7 mg/kg/day, I.V. (divided into 2 doses, every 12 hours).

According to the clinical response and the results of blood cultures, antibiotic therapy can be modified. Penicillin G can be substituted with apmicillin and gentamicin can be substituted with a more potent aminoglycoside as amikacin. Vancomycin (40-60 mg/kg/day, I.V., in 2-3 divided doses) is the drug of choice for methicillin-resistant staphylococci. Therapy should be continued for at least, 6 weeks to ensure complete organization of vegetations. A more prolonged course for 8 weeks can be expected in resistant cases.

3. Treatment of congestive heart failure: When infective endo-carditis is complicated with heart failure, conventional therapy with digoxin, diuretics and oxygen is indicated. In case of intractable heart failure due to severe valvular involvement, surgical removal of the vegetations may be life saving.

Prophylaxis against infective endocarditis

In patients with pre-existing cardiac disease, prophylaxis against infective endocarditis is recommended before dental procedures or surgery. Such prophylaxis can be made with a short course of antibiotics for few days, starting few hours before procedures. In case of dental surgery, oral penicillin or erythromycin is sufficient. With abdominal or urinary surgery, parenteral ampicillin and gentamicin is recommended.

5. Pericarditis

Pericarditis may accompany several infectious (viral, bacterial, tuberculous), inflammatory (rheumatic, rheumatoid, systemic lupus) and metabolic (uremia) conditions. With clinical suspicion, echocardiography is reliable for diagnosis and for evaluation of the size and progress of the pericardial effusion.

Treatment of pericarditis depends on the causative disease as well as the degree of pericardial involvement.

1. Acute viral (benign) pericarditis: As the illness is usually mild and pain is the main complaint, treatment with analgesics (Aspirin) is usually sufficient and the patient will recover over several weeks. In exceptionally severe cases with chronic relapsing course, prolonged therapy with potent anti-inflammatory drugs is indicated. Indomethacin (2 mg/kg /day, oral, in 2-3 divided doses) and prednisone (2 mg/kg/day, oral, in divided doses) are the most commonly used drugs.

2. Purulent pericarditis: Patients with this serious, potentially fatal, illness should be immediately hospitalized. Pericardiocenthesis (closed pericardial aspiration) is important for symptomatic relief and for culture and sensitivity studies. Prolonged parenteral antibiotic therapy for weeks is essential. Drugs similar to those used in infective endocarditis can be given. In severe cases with evident features of cardiac compression (acute cardiac tamponade), open pericardial drainage may be necessary.

3. Tuberculous pericarditis: The condition may occur secondary to rupture of a mediastinal lymph node into a pericardial space or due to hematogenous spread. Treatment is for 12-18 months with isoniazid (15-20 mg/kg/day, oral) and rifampicin (15 - 20 mg/kg/day, oral). Initial short course of corticosteroids is important to prevent constrictive pericarditis.

4. Constrictive pericarditis: It may occur as a late complication of purulent or tuberculous pericarditis. The condition responds dramatically to surgical radical pericardiotomy with decortication of the pericardium over a wide area of the heart.

5. Pericarditis of rheumatic diseases: Treatment is essentially directed to the causative disease. Rheumatic fever, rheumatoid arthritis and systemic lupus erythematosus are the main causes.

6. Acute Congestive Heart Failure

Acute congestive heart failure may occur in several clinical situations. In patients without pre-existing cardiac disease, severe myocarditis (viral, bacterial or rheumatic), paroxysmal atrial tachycardia, hypertensive crisis and acute renal failure are the main causes. Episodes of acute heart failure are also common with congenital or rheumatic heart diseases and the attacks are usually precipitated by respiratory infections, infective endocarditis or rheumatic activity.

Patients with acute congestive heart failure should be hospitalized, preferably in an intensive care unit. Close observation and frequent monitoring of vital signs, degree of distress, colour and level of consciousness are essential.

A) Treatment of failure

Management of acute congestive heart failure includes the following:

1. Bed rest: Complete bed rest is indicated during the early critical stage. Most patients prefer the semi-sitting position. Activity can be gradually allowed after adequate control of the condition.

2. Feeding: In severe cases accompanied with significant respiratory distress, oral feeding is hazardous especially in infants because of the risk of aspiration. Maintenance I.V. fluid therapy is mostly required during the first few days and the amount given per day should only equal 65 - 70% of the calculated amount. (See I.V. fluid therapy). With persistent significant distress after the first few days of therapy, nasogastric tube feeding should gradually replace the I.V. fluids. Oral feeding can be resumed gradually as soon as the condition allows. In older children with mild failure, oral feeding can be allowed from the start.

3. Oxygen therapy: All patients with acute congestive failure should receive oxygen. The method of administration depends on the age of the patient. Infants can be successfully managed with the head box while older children can receive oxygen with oxygen masks or nasal prongs. Initial oxygen concentration of 40% is usually sufficient. Oxygen should be given continuously and should be withdrawn gradually.

4. Digoxin therapy: Parenteral digoxin therapy (I.M. or preferably I.V.) is indicated in severe cases. The digitalizing dose (0.05 mg/kg) is divided into 3 doses (1/2, 1/4, 1/4 or 1/3, 1/3, 1/3). After the initial dose, the second and third doses are given after 8 hours and 16 hours respectively. In older children, the digitalizing dose should not exceed the adult dose (1.5 mg). The maintenance dose (0.01 mg/kg or 1/4 digitalizing dose) should start 24 hours after the initial digitalizing dose and should be divided into 2 equal doses (every 12 hours).

As soon as the patient can tolerate oral feeding, the maintenance dose should be given orally. Duration of therapy depends mainly on the causative disease. It may be as short as few days (paroxysmal atrial tachycardia) or as long as several weeks (rheumatic carditis). Signs of digitalis toxicity should be in mind.

5. Diuretics: They act as a preload reducing agent, as they reduce the circulating blood volume through diuresis. Furosemide, the most commonly used drug, is given initially in a dose of 1-2 mg/kg I.V. The dose can be repeated after 12 hours if manifestations of pulmonary congestion are prominent. With adequate control of the condition, the drug can be given orally in a dose of 1-2 mg/kg/day (see diuretics).

6. Treatment of pulmonary edema: Patients with severe respiratory distress should be transferred to ICU where facilities for blood gas analysis and assisted ventilation are available.

(a) Initial measures: Increase oxygen concentration to 60-70% and give furosemide I.V. in a dose of 2 mg/kg/dose every 12 hours.

(b) Continuous positive airway pressure (CPAP): Persistent hypoxemia (low PaO_2 and low saturation below 90%) in spite of high oxygen and diuretic therapy is an indication for endotracheal intubation and continuous positive airway pressure.

(c) Mechanical ventilation: In advanced cases complicated with respiratory failure (PaO_2 below 50 mmHg and $PaCO_2$ above 60 mmHg) in spite of the above measures, mechanical ventilation is indicated and may be life saving.

7. Treatment of cardiogenic shock: In severe cases not responding to conventional measures or when manifestations of cardiogenic shock appear (hypotension and poor peripheral perfusion), treatment with inotropic catecholamines (dopamine and/or dobutamine) is indicated. The use of these serious drugs should be limited to patients in intensive care units where continuous monitoring of the heart is essential. **Dopamine** is given initially by continuous infusion in a dose of 2-10 mcg/kg/minute. **Dobutamine** can be added in a dose of 5-20 mcg/kg/minute when dopamine alone is not effective. As dobutamine has a less prominent chronotropic effect, it is the preferable initial drug when a marked tachycardia is present (See inotropic drugs for dilution and infusion rate).

B) Treatment of the cause

Specific therapy of the causative disease is an integral part of successful therapy. Myocarditis, infective endocarditis, rheumatic activity, acute renal failure, hypertensive crisis or paroxysmal atrial tachycardia should be treated with the appropriate lines of therapy.

7. Chronic Congestive Heart Failure

Chronic congestive heart failure may complicate several congenital or acquired cardiac diseases. Congenital non-cyanotic heart diseases with left to right shunt (as big VSD and PDA) are the main causes in infancy and early childhood, while chronic rheumatic heart disease is the main cause in school age children. Congestive cardiomyopathy should be considered in infants and children with chronic CHF without evident congenital or rheumatic heart disease.

Clinical manifestations usually appear insidiously over several weeks or months. Feeding difficulties in infants and exercise intolerance in children are the main early symptoms (History is extremely important). In more severe cases, manifestations of pulmonary congestion (dyspnea on mild exertion and orthopnea) and systemic congestion (hepatomegaly, pulsating neck veins and oedema) start to appear. In advanced cases, ascites may become evident.

Unlike acute congestive heart failure that necessitates hospitalization and urgent parenteral therapy, chronic congestive heart failure can be managed on an **outpatient basis with oral drugs.** Management includes the following:

1. Physical activity: In infants, feeding difficulties are the main problem and fractionation of feeding into small frequent feeds is important to avoid fatigue and aspiration. In children, some restriction of physical activity is required and competitive sports should be avoided. Fortunately, the child will naturally tend to limit his activity according to his ability. In severe cases, most patients prefer the semisitting position.

2. Diet: An adequate well balanced diet is important to provide sufficient calories. Low salt diet is generally recommended especially when manifestations of pulmonary and systemic congestion are evident.

3. Drug therapy: Chronic oral digoxin therapy is the main treatment. Drugs as diuretics or afterload-reducing agents may be added in severe cases.

(a) Oral digoxin therapy: Digoxin is given orally in a dose of 0.01 mg/kg/day divided into 2 equal doses (without initial digitalization). With this schedule, full digitalization is usually achieved over 7 -10 days. For older children (above 6 years), the total daily dose should not exceed 0.2 - 0.5 mg/day. Infants and young children can receive the solution form ***(Lanoxin pediatric elixir, 0.05 mg/ml)*** while older children can take the tablet form ***(Lanoxin or Cardixin tablets, 0.25mg).*** Clinical response to digoxin therapy may take few weeks to appear. Dosage can be slightly adjusted according to the response. Parents should be oriented with early signs of digitalis toxicity (anorexia, nausea and vomiting) and the drug should be immediately discontinued on clinical suspicion.

Also, it is important to remember that the drug should be always kept out of reach of the child (See inotropic drugs).

(b) Oral furosemide therapy: Chronic oral furosemide therapy may be added in cases not adequately responding to digoxin therapy or when manifestations of pulmonary and systemic congestion are evident. It is given in a dose of 1 - 4 mg/kg/day or every other day as a single morning dose. Treatment should start with low dosage. The drug is only available in tablet form *(Lasix or Salex tablets, 40 mg)*. Chronic potassium chloride supplementation is usually needed especially with high daily dosage *(Potassium chloride syrup, 10 mEq/5 ml)*. It is given in a dose of 1 - 2 mEq/kg/day.

(c) Oral afterload reducing agents: These drugs are mainly useful in case of congestive cardiomyopathy or in patients with severe mitral regurgitation or aortic insufficiency. **Captopril** ***(Capoten tablets, 25 mg)*** is the mainly used drug. It is given orally in a dose of 0.5-5 mg/kg/day, divided into 2-4 equal doses. Treatment should start with low dosage to avoid hypotension. As the drug also interferes with aldosterone production, it has the advantage of controlling salt and water retention. Alternatively, other drugs as **hydralazine** *(Apresoline)* or **prazosin** *(Minipress)* can be used (See antihypertensive drugs).

4. **Surgical treatment:** Surgery should be considered in severe cases, with marked dyspnea on mild exertion, and in progressive failure:

- In congenital heart disease: Corrective surgery.
- In chronic rheumatic heart disease: Valvotomy for severe stenotic lesions and valve replacement for severe regurgitation.
- In progressive congestive cardiomyopathy: Cardiac transplantation.

Practical examples

1. **A child, 6 years old (20 kg) with moderate chronic congestive heart failure.**

    RI Digoxin OR Cardixin tablets (0.25 mg).
    Half a tablet, twice daily (morning and evening).

    RI Lasix OR Salex tablets (40 mg).
    One tablet in the morning every other day.

    RI Potassium chloride syrup (10 mEq/5 ml).
    One teaspoon, twice daily.

2. **A child, 8 years old (25 kg) with severe chronic congestive heart failure, not adequately responding to digoxin and furosemide therapy.**

    Add:
    RI Capoten tablets (25 mg).
    Half a tablet, twice daily.

6

Respiratory System

1. Nasopharyngitis.
2. Sinusitis.
3. Otitis Media.
4. Tonsillitis.
5. Acute Bronchitis.
6. Whooping Cough.
7. Acute Laryngitis.
8. Pneumonias.
9. Acute Bronchiolitis.
10. Bronchial Asthma.
11. Pulmonary Tuberculosis.

1. Nasopharyngitis (Common Cold)

Management of acute viral nasopharyngitis is mainly symptomatic.

1. Nasal decongestants: These drugs are usually needed especially in severe cases in which nasal obstruction interferes with food intake and sleep. It is important to remember that the duration of therapy should not exceed 4-5 days; otherwise, these drugs will induce chemical rhinitis and continuation of symptoms. Both nose drops and oral preparations are available. (See nasal decongestants).

(a) Nose drops: They commonly cause local irritation, so, their use should be limited to cases with severe obstruction and when oral preparations are contraindicated (as nasopharyngitis with bronchitis). The dose is 1-2 drops, instilled in each nostril, 10 minutes before feeding, 2-3 times per day. Prior clearing of the nose with a cotton bud or suction with a soft bulb syringe may be required in cases with severe obstruction.

(b) Oral nasal decongestants: These preparations don't cause local irritation and they induce shrinkage of the congested mucosa of the sinuses as well. The major disadvantage is that they also induce dryness of bronchial secretions, so they are contraindicated when nasopharyngitis is complicated with bronchitis. The daily dose is divided into 3 - 4 doses.

2. Analgesics and antipyretics: Paracetamol or ibuprofen is usually needed for associated fever and to reduce aching and irritability. Some oral decongestants contain paracetamol as well. Aspirin should be avoided in respiratory viral infections because of the risk of Reye syndrome.

3. Antibiotics: The use of antibiotics should be limited to cases with bacterial complications as otitis media or sinusitis.

4. Orientation of parents: Excess fluid intake is important. The transient anorexia is common and the child should not be forced to eat. The old folkloric view of avoiding some foods (as eggs) is not scientific. Parents should realize that the symptoms of common cold might last for as long as two weeks. Failure to provide such an explanation will result in multiple unnecessary visits.

Remarks

- Exclusion of other causes of nasal discharge is essential.
- History of asthma is important, as nasopharyngitis may be the early triggering stimulus for an asthmatic attack.
- Nasopharyngitis may be just an initial manifestation of a more serious coming disease as bacterial pneumonia, acute bronchiolitis, pertussis or measles.

Practical examples

1. An infant, 4 months old (6 kg) with acute nasopharyngitis and fever (38.5°C).

Rl Rhinomol OR Flumol syrup

1/2 teaspoon (2.5 ml), oral, 3 times daily for 4 - 5 days.

Both Rhinomol and Flumol contain paracetamol as well (120 mg/5 ml).

2. An infant, 1 year old (9 kg) with acute nasopharyngitis (severe obstruction).

Rl Otrivin pediatric OR Iliadin pediatric nasal drops.

1 - 2 drops, instilled in each nostril, 2 - 3 times per day, for 3 - 4 days only.

Rl Flumol OR Congestal OR Michaelon syrup

3/4 teaspoon (3.5 ml), oral, 3 times daily for 4 – 5 days.

The above 3 preparations contain paracetamol as well.

3. A child, 3 years old (15 kg) with acute nasopharyngitis and fever

Rl Flumol syrup ((15 mg + 120 mg paracetamol/5 ml).

One teaspoon (5 ml), oral, 3 times daily for 4 - 5 days.
(Dose is 3-4 mg/kg/day divided into 3 doses).

OR

Rl Congestal syrup ((15 mg + 160 mg paracetamol/5 ml).

One teaspoon (5 ml), oral, 3 times daily for 4 - 5 days.
(Dose is 3-4 mg/kg/day divided into 3 doses).

OR

Rl Michaelon syrup ((30 mg + 125 mg paracetamol /5 ml).

One teaspoon (5 ml), oral, 3 times daily for 4 - 5 days.
(Dose is 3-4 mg/kg/day divided into 3 doses).

OR

Rl Brufen Flu syrup (15 mg + 100 mg ibuprofen /5 ml).

One teaspoon (5 ml), oral, 3 times daily for 4 - 5 days.
(Dose is 3-4 mg/kg/day divided into 3 doses).

OR

Rl Dolo-D syrup (15 mg + 100 mg ibuprofen /5 ml).

One teaspoon (5 ml), oral, 3 times daily for 4 - 5 days.
(Dose is 3-4 mg/kg/day divided into 3 doses).

(All above 5 preparations contain Pseudoephedrine as a nasal decongestant).

2. Acute Sinusitis

Viral nasopharyngitis commonly spreads to involve the paranasal sinuses but this usually subsides within 2- 3 days without treatment. However, secondary bacterial infection of sinuses may occur and results in persistence of purulent nasal discharge, high fever or persistent night cough. Management includes:

1. Antibiotic therapy: An oral broad-spectrum antibiotic for 10-14 days is indicated for control and eradication of bacterial infection. Choices are:

- **Broad-spectrum penicillins** as ampicillin or amoxicillin (50 -100 mg/kg /day). The newer drugs as sultamicillin (ampicillin + sulbactam) or co-amoxiclav (amoxicillin + clavulanic acid) are more effective than either drug alone.
- **Second-generation cephalosporins** as cefuroxime, cefaclor or cefprozil (40 mg/kg/day) are also very effective.
- **New macrolides** as clarithromycin or azithromycin can be also used.

2. Nasal decongestants: Oral nasal decongestants can be used in the first 4 - 5 days of therapy to reduce sinus congestion.

3. Analgesics and antipyretics: Paracetamol or other antipyretics may be needed in the first few days to control fever and pain.

4. Surgical drainage of the sinuses is almost never required in children.

Practical example

A child, 6 years old (20 kg) with acute purulent sinusitis.

RI Amoxil OR E-mox oral suspension (250 mg/5 ml).
One and half teaspoon (7.5 ml), every 8 hours for 10 days.

OR RI Augmentin OR Curam suspension (457 mg/5 ml).
One teaspoon (5 ml), every 12 hours for 10 days.

OR RI Cefzil suspension (250 mg/5 ml).
One and half teaspoon (7.5 ml), every 12 hours for 10 days.

OR RI Ceclor OR Bacticlor suspension (250 mg/5 ml).
One and half teaspoon (7.5 ml), every 12 hours for 10 days.

OR RI Klacid suspension (250 mg/5 ml).
One teaspoon (5 ml), every 12 hours for 10 days.

\+ ***RI Flumol OR Congestal syrup (15 mg/5 ml)***
One teaspoon (5 ml), oral, 3 times daily for 4 days.

Notice: Flumol and Congestal contain paracetamol as well (120 mg/5 ml and 160 mg/5 ml respectively).

3. Acute Otitis Media

(6month → 6years)

Acute inflammation of the middle ear is a common complication of acute nasopharyngitis especially in late infancy and early childhood. Unexplained crying and irritability in a febrile infant or a child should raise the possibility. Examination of eardrums with an otoscope is essential for diagnosis.

Management of acute otitis media includes:

1. Antibiotic therapy: The use of a broad-spectrum antibiotic for 7 - 10 days is important for control and eradication of infection. The choices of antibiotics and dosage are the same as those for acute sinusitis.

2. Nasal decongestants: These drugs may be needed in the first 3 - 4 days of therapy to relieve eustachian obstruction and to control the associated nasopharyngitis. (see nasopharyngitis).

3. Analgesics and antipyretics: Paracetamol, or other antipyretics, can be used to control fever and earache. The earache usually disappears within 1 - 2 days of therapy. Analgesic eardrops ***(Otocalm drops)*** may be also used.

4. Myringotomy: It is rarely indicated in children. Persistent severe earache for more than 2 days is the main indication. However, some patients present initially with a spontaneous perforation and purulent ear discharge. In these cases, antibiotic eardrops (as ***Polyspectran eye/ear drops)*** for 5 days are added.

Practical example

An infant, 1 year old (10 kg) with acute otitis media.

R/ Augmentin OR Curam OR E-moxclav suspension (156 mg/5 ml).
One teaspoon (5 ml), every 8 hours for 7 days.

OR ***R/ Ceclor OR Bacticlor suspension (125 mg/5 ml).***
One teaspoon (5 ml), every 8 hours, for 7 days.

OR ***R/ Cefzil suspension (125 mg/5 ml).***
One and half teaspoon (7.5 ml), every 12 hours for 7 days.

OR ***R/ Zithromax OR Zithrone OR Aziwok suspension (200 mg/5 ml).***
1/2 teaspoon (2.5 ml), once daily for 6 days.

\+ ***R/ Rhinomol Syrup (5 mg/5 ml).***
One teaspoon (5 ml) oral, 3 times daily for 3 - 4 days.

\+ ***Re-examination after one week.***

4. Streptococcal Pharyngitis (Tonsillitis)

Acute bacterial infection of the pharynx and tonsils is common in children, but rare in infants. Differentiation from other causes of sore throat is important.

Management of streptococcal pharyngitis includes:

1. Antibiotic therapy: An oral antibiotic for a full course of 10 days is important for complete eradication of the organism especially in areas where rheumatic fever is still common. There are 3 choices:

- **Erythromycin** (50 mg/kg/day) divided into 3-4 doses. Newer macrolides as clarithromycin (15 mg/kg/day), roxithromycin (5-8 mg/kg/day) or azithromycin (10 mg/kg/day) can be also used.
- **First-generation cephalosporins** as cephalexin, cephradine or cefadroxil (50 mg/ kg/day) divided into 3-4 doses. These drugs are probably more effective than oral penicillin or erythromycin.
- **Oral penicillin V** (Phenoxymethyl penicillin) in a dose of 50.000 unit/kg/day divided into 3-4 doses. It is important to remember that broad-spectrum penicillins as ampicillin or amoxycillin are not a good choice because oral penicillin (phenoxymethyl penicillin) is 10 times more effective. Also, the silly mistake of prescribing an aminoglycoside injection as gentamicin or tobramycin should be avoided, as these drugs have no effect on streptococci.

2. Analgesics and antipyretics: Paracetamol or other antipyretics are usually needed during the first few days to control fever and sore throat. Fever usually subsides within few days, but it may remain as long as 5 days.

3. Orientation of parents: Many parents do not take it seriously and will discontinue the antibiotic as soon as the fever subsides. Parents should realize that a full course is important to prevent recurrence and to minimize the risk of late complications as rheumatic fever and post-streptococcal glomerulonephritis. Some children find it difficult to swallow solid foods, so excess liquids should be encouraged.

What are the indications for adenotonsillectomy?

The widespread mistake of advising tonsillectomy for vague reasons as poor appetite or recurrent fever should be avoided. Physicians should generally hesitate to advise tonsillectomy. Any of the following criteria may be considered as an indication for surgery:

1. Unusually recurrent tonsillitis: More than 5 documented attacks per year.
2. Chronic tonsillitis: Persistent hyperemia of the anterior pillars, persistent enlargement of cervical lymph nodes or persistent follicular tonsillitis with cheesy material within the crypts. It is important to remember that the size of tonsils is not important. Normal tonsils in children are relatively larger and may even meet in the midline. On the other hand, chronically infected tonsils may be smaller than average.
3. Peritonsillar abscess.
4. Symptomatic adenoid hypertrophy: Persistent mouth breathing, snoring, nasal speech, persistent nasopharyngitis or repeated attacks of otitis media.
5. Previous documented history of rheumatic fever.

In general, tonsillectomy should not be done before the age of 4 years and should be postponed for 3 weeks after recovery from the acute infection.

Practical example

A child, 6 years old (20 kg) with streptococcal pharyngitis.

OR RI Erythrocin OR Erythrin oral suspension (200 mg/5 ml).
Two teaspoons (10 ml), oral, every 8 hours (7 a.m., 3 p.m. and 11 p.m) for 10 days.

OR RI Klacid suspension (250 mg/5 ml).
One teaspoon (5 ml), oral, every 12 hours for 7 days.

OR RI Zithromax OR Xithrone suspension (200 mg/5ml).
One teaspoon (5 ml), once daily for 3 days only.

OR RI Ceporex OR Ospexin OR Keflex suspension (250 mg/5 ml).
One teaspoon (5 ml), oral, every 8 hours, for 7 days.

OR RI Duricef OR Ibidroxil OR Biodroxil suspension (250 mg/5 ml).
Two teaspoon (10 ml), oral, every 12 hours, for 7 days.

OR RI Ospen oral suspension (400.000 unit/5 ml).
One teaspoon (5 ml), oral, every 8 hours (7 a.m., 3 p.m. and 11 p.m) for 10 days.

\+ ***RI Cetal OR Temporal suspension (250 mg/5 ml).***
One teaspoon (5 ml), oral, 4 times daily, for 2 - 3 days.

5. Acute Bronchitis

Most cases of acute tracheobronchitis recover spontaneously without any therapy. However, management may include the following aspects:

1. Antibiotic therapy: It is not indicated in every case as the great majority of cases are of viral origin. However, antibiotics can be used when the possibility of bacterial infection is considerable as in:

- Bronchitis in early infancy.
- Bronchitis in malnourished infants.
- When associated with high persistent fever.
- When associated with bacterial complications as sinusitis or otitis media.

The use of oral antibiotics as **broad-spectrum penicillins** (ampicillin or amoxycillin) or **first-generation cephalosporins** (cephalexin, cephradine or cefadroxil) is quite sufficient. **Second-generation cephalosporins** may be also used. Parenteral drugs are not indicated for this simple infection. Duration of therapy is usually 5-7 days. Longer therapy may be needed for associated sinusitis or otitis media.

2. Cough medicines: The value of these drugs is generally limited and they do not alter the natural course of illness. **Cough suppressants** (as pholcodine, noscapine, dextromethorphan or pipazethate) may be used in the first few days, especially at night, to induce a calm sleep. Once the cough becomes productive, these drugs are contraindicated. **Expectorants** are commonly prescribed for 5-7 days. However, the therapeutic value of these drugs is doubtful and the choice between the different innumerable preparations is not critical. Certainly, drinking water and other liquids is the best expectorant.

3. Other drugs: Antipyretics as paracetamol or ibuprofen can be used for fever. Nose drops may be used for associated nasopharyngitis. It is important to remember that the oral nasal decongestants are contraindicated in management of bronchitis as they will cause dryness of bronchial secretions.

4. Orientation of parents: Excess fluid intake is important to enhance expectoration. Lemon juice with honey may have some soothing effect. Feeding is better fractionated into small frequent feeds to minimize the post-tussive vomiting which is common in infants and young children. The associated anorexia is transient and the child should not be forced to eat. Parents should realize that the cough may continue as long as 2 weeks. Persistence of cough for more than 2 weeks should be taken with concern. Complications as sinusitis (important) or segmental collapse should be excluded.

Practical examples

1. **An infant, 4 months old (6 kg) with acute bronchitis.**

RI Hiconcil OR E-mox suspension (125 mg/5 ml).
One teaspoon (5 ml), oral, every 8 hours (7 a.m., 3 p.m. and 11 p.m.) for 7 days.

RI Ambroxol OR Mucosolvan OR Bronchopro OR Mucin drops.
6 drops, oral, 3 times daily, for one week.

2. **An infant, 1 year old (10 kg) with acute bronchitis. Temperature is 39.5°C and cough is severe at night.**

RI Ceporex OR Ospexin suspension (125 mg/5 ml).
One teaspoon (5 ml), every 8 hours (7 a.m., 3 p.m. and 11 p.m.) for 7 days.

OR RI Amoxil OR E-mox OR Hiconcil oral suspension (125 mg/5 ml).
One teaspoon (5 ml), every 8 hours, for 7 days.

OR RI Augmentin OR Curam suspension (156 mg/5 ml).
One teaspoon (5 ml), every 8 hours for 7 days.

OR RI Ceclor OR Bacticlor suspension (125 mg/5 ml).
One teaspoon (5 ml), every 8 hours, for 7 days.

OR RI Cefzil suspension (125 mg/5 ml).
One teaspoon (5 ml), every 12 hours, for 5 days.

\+ *RI Phenergan expectorant OR Toplexil OR Pulmocare syrup*
One teaspoon (5 ml), oral, 3 times daily for 7 days.

\+ *RI Pyral OR Paramol syrup (120 mg/5 ml).*
One teaspoon (5 ml), oral, 4 times daily (every 4 - 6 hours) or when temperature exceeds 38.0°C.

\+ *RI Selgon infantile supp. (10 mg).*
One suppository, rectal, once at night for 3 days.

3. **A chlid, 6 years old (20 kg) with acute bronchitis. No fever or associated complications.**

RI Osinex OR Toplexil OR Pulmocare OR Bronchophen syrup.
2 teaspoons (10 ml), oral, 3 times daily for 5 - 7 days.

OR NO MEDICATIONS.

6. Whooping Cough (Pertussis)

Whooping cough has become relatively uncommon, mostly because of the widespread application of compulsory vaccination. The relative risk to non-vaccinated children is 4 times when compared to fully vaccinated ones. As the immunity is not transferred across the placenta, even the newborn is at risk.

Management of pertussis includes the following aspects:

1. Proper nursing care: Infants under the age of 6 months usually need hospitalization to ensure close observation. During a paroxysm, the young infant should be held in a head down position until the spasm is over. In cases where the spasms are frequent, oxygen is needed. Older infants and children can be managed at home.

2. Antibiotic therapy: Erythromycin (50 mg/kg/day) for 10 days is effective in eradication of the organism and reduction of the period of infectivity. Antibiotic therapy will not shorten the duration of illness. New macrolides as clarithromycin, roxithromycin or azithromycin can be used as an alternative.

3. Cough suppressants: Although the response is not satisfactory, these drugs can be tried in severe cases with frequent paroxysms. As the drug may be used for weeks, codeine-containing preparations should be avoided because of the risk of habituation. Other drugs (as pholcodine, noscapine, dextromethorphan or pipazethate) can be used. The daily dose is divided into 2 - 4 doses. The night dose should be bigger or a suppository can be used at night.

4. Orientation of parents: Parents should realize that no medication will shorten the duration of illness and the patient will continue to cough for several weeks. Small frequent feeds are important to minimize the post-tussive vomiting. Avoidance of exposure to respiratory infections is very important. Mild infections as nasopharyngitis may worsen the condition and prolong the duration of illness. The patient is infectious from the catarrhal stage and up to 3 -4 weeks. With erythromycin therapy, infectivity period becomes 7 days only. Susceptible unvaccinated infants are at great risk and should be protected from exposure (the attack rate, or the possibility of being infected, is 97-100%). These exposed infants should receive an oral course of erythromycin for 10 days and should start vaccination. Vaccinated siblings or other close contacts below the age of 7 years should also receive erythromycin for 10 days and a booster dose of D.P.T. Parents or other contacts should also receive erythromycin for 10 days or until the patient has received erythromycin for 7 days.

5. Treatment of complications: Pneumonia is the most common complication and the main cause of death in fatal cases. As it is commonly

caused by secondary bacterial infections, appropriate parenteral antibiotic therapy for 10 days is important (see pneumonia). Convulsions and tetanic spasms should be controlled with the anticonvulsants and I.V. calcium gluconate.

Practical examples

1. An infant, 4 months old (6 kg) with whooping cough.

Hospitalization +

RI Erythrocin OR Erythrin suspension (200 mg/5 ml).
1/2 teaspoon (2.5 ml), oral, every 8 hours (7 a.m., 3 p.m. and 11 p.m.) for 10 days.

OR RI Zithromax OR Zithrone suspension (200 mg/5 ml).
1/2 teaspoon (2.5 ml) once daily for 6 days.

\+ *RI Silomat drops (2 mg/drop).*
2 drops, oral, 3 times daily. Night dose can be 3 drops.

OR RI Selgon drops (2 mg/drop).
2 drops, oral, 3 times daily. Night dose can be 3 drops.

2. A child 2 years old (12 kg) with whooping cough.

RI Erythrocin OR Erythrin suspension (200 mg/5 ml).
One teaspoon (5 ml), oral, every 8 hours (7 a.m., 3 p.m. and 11 p.m.) for 10 days.

RI Sinecod syrup (7.5 mg/5 ml).
One teaspoon, oral, 3 times daily.

RI Eucaphol ped. supp. (5 mg) OR Selgon ped. supp. (10 mg).
One suppository, rectal, once at night.

3. A child, 6 years old (20 kg) with whooping cough.

RI Erythrocin OR Erythrin suspension (200 mg/5 ml).
One and half teaspoon (7.5 ml), oral, every 8 hours (7 a.m., 3 p.m. and 11 p.m.) for 10 days.

OR RI Klacid suspension (250 mg/5 ml).
One teaspoon (5 ml), oral, every 12 hours for 6 days.

\+ *RI Silomat syrup (20 mg/5 ml).*
One teaspoon (5 ml), oral, 3 times daily.

7. Acute Laryngitis (Infectious Croup)

Management of acute laryngeal stridor depends on the degree of airway obstruction, the age of the patient and the causative disease.

The essential initial step in management is the clinical decision of whether the case is for hospital or home management.

A) Home management

Most afebrile patients with mild infectious laryngitis, mild laryngo-tracheobronchitis or spasmodic laryngitis can be safely managed at home.
Management may include:

1. Warm moist environment: This can be provided by taking the child into a bathroom and turning on the hot shower or hot taps. Inhalation of the hot steam will usually relieve minor obstruction within 30- 60 minutes.

2. Drug therapy: No medication can favorably alter the course of illness. However, a broad-spectrum antibiotic (as ampicillin) and oral steroids (as dexamethasone) may be used in borderline moderate cases to minimize the necessity for hospitalization. Expectorants or mucolytics may be also used in laryngotracheobronchitis.

B) Hospital management

Hospitalization is indicated in the following conditions:
- Any infant with grade II stridor (stridor at rest).
- Any child with grade III stridor (stridor with retractions).
- Suspected bacterial disease as in those with high fever and severe obstruction.
- Grade IV stridor (Stridor with cyanosis and/or altered consciousness) is an indication for immediate hospitalization and endotracheal intubation.

Hospital management includes the following aspects:

1. Close observation: Frequent monitoring of the heart rate, respiratory rate, degree of retraction, colour and level of consciousness is very essential to assess the course of illness and to identify those in need of endotracheal intubation.

2. Minimal disturbance: Nursing and medical procedures that disturb the child or increase anxiety should be minimized. The mother should remain beside him for reassurance, at least until he sleeps.

3. Humidification: Warm moist atmosphere is generally useful. Inhalation of warm water vapour may be helpful in relieving the laryngeal obstruction, although the mechanism of action is unknown. Ultrasonic nebulizer, if available, is frequently effective within 20 - 30 minutes.

4. Drug therapy: It may include:

(a) Corticosteroids: Although their use is controversial, they should be tried in severe cases. Hydrocortisone (10 mg/kg/dose, I.V., every 6 hours) or dexamethasone (0.25 mg/kg/dose, I.V or I.M, every 12 hours) can be used for 2-3 days.

(b) Antibiotics: Parenteral antibiotic therapy is important when bacterial origin is suspected especially in those with high fever. The choices are:

— Ampicillin (100 mg/kg/day ... I.V., divided into 4 doses).
  (Ampicillin can be replaced with new drugs as sultamicillin or co-amoxiclav).
— Cefotaxime (50 mg/kg/day ... I.V divided into 2 doses).
  Duration of therapy is usually 5 - 7 days.

(c) Sedatives and bronchodilators are contraindicated. Sedatives will impair consciousness and bronchodilators increase oxygen requirements.

5. Oxygen therapy: Although it is important to relieve hypoxia, it has 2 main disadvantages. First, it delays the appearance of cyanosis, which is an important indication for endotracheal intubation. Second, it is commonly rejected by the child and makes him more upset. However, oxygen can be used if the patient tolerates it and if observation is too close.

6. Feeding: Maintenance I.V. fluid therapy is usually needed during the first 24 hours. Careful oral intake is usually initiated from the second day.

7. Mechanical relief of obstruction: Fortunately, 98% of cases improve within 48 hours with the above-mentioned lines of therapy. In 2% of cases, endotracheal intubation is necessary to relieve the severe obstruction. The main indications are cyanosis, altered consciousness, extreme restlessness or gradual progression of the degree of airway obstruction.

Practical example

An infant, one year old (10 kg) with severe laryngeal stridor. No cyanosis or altered consciousness.

Hospitalization.

+ *Monitoring:* H.R., R.R., retractions, colour, level of consciousness and arterial oxygen saturation every hour.
+ *Drugs:* - Ampicillin : 250 mg ... I.V, every 6 hours.
  - Hydrocortisone: 100 mg ... I.V, every 6 hours.
+ *I.V. fluids:* Kadalex 800 ml, Saline 200 ml | over 24 hours. (about 13 drops/minute)
  (Careful oral intake from the second day).
+ *Ultrasonic nebulization:* For 30 minutes every 3 hours.
+ *Oxygen therapy:* 40 % oxygen in a head box (if tolerated).

8. Pneumonias

Pneumonia is one of the most frequent emergencies in infancy and early childhood. Clinical diagnosis should include the pathological type, the possible causative organism as well as the associated complications. The clinical decision regarding the place and lines of management depends on the age of the patient, pathological type, degree of distress and presence or absence of complications.

A) Hospital management

Presence of respiratory distress is the main indication for hospitalization. Most infants and young children with pneumonia are distressed and need admission. Hospital management includes the following aspects:

1. Close observation: Frequent monitoring of the degree of respiratory distress is essential. Respiratory rate, retractions, grunting, colour and level of consciousness should be recorded every 1 - 2 hours. Continuous monitoring of arterial oxygen saturation with pulse oxymeter, if available, is very helpful.

2. Initial investigations: Complete blood count (CBC) and C-reactive protein (CRP) are important to differentiate bacterial from viral infections. Chest x-ray is also essential. Continuous or repeated measurement of arterial oxygen saturation is important. Arterial or arterialized blood gases (ABG), if available, is also important to assess the degree of hypoxemia and ventilatory functions. PaO_2 below 50 mm Hg indicates respiratory failure. Repeated measurement of ABG is particularly important in infants with severe bronchopneumonia. $PaCO_2$ above 60 mmHg is an indication for mechanical ventilation.

3. Oxygen therapy: Presence of respiratory distress is an indication for oxygen therapy. The method of administration depends on the age as well as the patient's tolerance. Infants can be successfully managed with the head box, while older children can receive oxygen with oxygen mask or nasal prongs. The concentration of oxygen required depends on the degree of respiratory distress and the level of PaO_2. Practically, 40 - 60% oxygen is usually sufficient, and the subsequent changes will depend on the course of illness.

4. Antibiotic therapy: All cases of severe pneumonia should be considered potentially bacterial and should receive parenteral antibiotics for 10 days.
* In infants and young children, a combination of two parenteral drugs seems reasonable. Ampicillin (100 mg/kg/day) and an aminoglycoside as gentamicin (6 mg/kg/day) are a satisfactory initial therapy.
* As an alternative, parenteral second generation cephalosporin as cefuroxime (75-150 mg/kg/day) is recommended.
* In severe fulminant cases of bronchopneumonia, one of the third generation cephalosporins as cefotaxime or cefoperazone (100-200 mg/kg/day) can be used.

* When the possibility of staphylococcal pneumonia is standing (empyema, pneumatoceles), parenteral vancomycin or clindamycin should be added.
* The subsequent change of antibiotic therapy depends on the clinical response and the result of sputum culture. The intravenous route is the preferable one, but I.M. injections can be also effective.

5. I.V. fluid therapy: In infants with moderate or severe distress, oral feeding is hazardous and may lead to serious aspiration. Maintenance I.V. fluid therapy is usually needed during the first 2 - 3 days to provide an adequate fluid intake. If the patient is still having a significant distress, nasogastric tube feeding should gradually replace the I.V. fluid therapy. Oral feeding can be resumed in patients with no or minimal distress. The common mistake of allowing oral feeding to severely distressed infants should be avoided. On the other hand, I.V. fluids only for more than 3 days should be also avoided.

6. Management of complications: The main complications are pleural effusion, respiratory failure, congestive heart failure and paralytic ileus.

(a) Pleural effusion (Empyema): With clinical suspicion, radiological confirmation and diagnostic aspiration are the initial steps and the sample should be sent for culture and sensitivity studies. Closed intercostal drainage (under water seal) is then indicated in cases with massive or moderate effusion and the tube is left in place until complete drainage and complete expansion of the collapsed lung which is usually achieved within 2-5 days. In cases complicated with bronchopleural fistula, the tube should be left until complete healing of the fistula, which may occur over few weeks. The diagnosis of bronchopleural fistula depends on observation of "bubbling" in the glass of the under water seal during crying or deep respiration. It is important to mention that the ultimate prognosis of empyema in children is excellent and chest surgery is almost never necessary. Even in cases complicated with pleural thickening, fibrothorax or chest deformity, complete recovery will occur over few months.

(b) Respiratory failure: Fortunately, most cases of pneumonia with respiratory failure respond to management and recover completely in 7-10 days. In exceptionally severe cases of bronchopneumonia in infants, assisted mechanical ventilation is frequently lifesaving. The clinical criteria to initiate mechanical ventilation are cyanosis (in spite of 60% oxygen) or progressive deterioration of the level of consciousness. On laboratory level, arterial saturation below 90% or PaO_2 below 50 mm Hg (with 60% oxygen) or $PaCO_2$ above 60 mm Hg are indications for mechanical ventilation. When facilities for intensive care are not available, manual ventilation with the bag and mask is an alternative.

(c) Congestive heart failure: Myocarditis and heart failure may occur especially in infants with severe bacterial bronchopneumonia. Parenteral digoxin therapy (loading and maintenance) is indicated for 2-4 days. The total fluid intake should be reduced by about 20 - 30%.

(d) Paralytic ileus: Severe pneumonia is the commonest cause of reflex ileus in infants. Vomiting and abdominal distension are the main clinical findings. Plain X-ray on the abdomen (in erect position) will show multiple fluid levels. The patient should be kept on maintenance I.V. fluid therapy with complete rest of the gastrointestinal tract. The condition usually subsides within few days and gradual oral feeding can be resumed.

B) Home management

Children above the age of 4 - 6 years with lobar pneumonia and without an evident distress or complications can be managed at home as those with severe bacterial bronchitis. Oral sultamicillin ***(Unasyn)*** or co-amoxiclav ***(Augmentin)*** for 10 days is satisfactory. An oral second-generation cephalosporin as cefuroxime ***(Zinnat)*** or cefaclor ***(Ceclor or Bacticlor)*** is an alternative. When mycoplasma pneumonia is considered, oral macrolide as azithromycin ***(Zithromax)*** or clarithromycin ***(Klacid)*** can be used.

Practical example

An infant, 6 months old (7 kg) with severe bronchopneumonia.

Hospitalization.

+ ***Close observation:*** H.R., R.R., retractions, colour, level of consciousness and arterial oxygen saturation every hour.
+ ***Investigations:*** CBC, CRP, ABG and Chest x-ray.
+ ***Oxygen therapy:*** 60% in a head box.
+ ***I.V. fluid therapy:*** - Kadalex: 600 ml | over 24 hours
  - Saline: 150 ml | (10 drops/minute)

  (To be repeated on the second day and then gradually replaced by naso-gastric tube feeding or oral feeding according to the degree of distress).
  e.g. : On the third day (with significant distress), fluid intake is as follows:

  (a) I.V. fluids: - Kadalex: 300 ml | over 24 hours
  - Saline: 75 ml | (5 drops/minute)

  (b) Nasogastric tube feeding: 60 ml of a full strength humanized formula every 3 hours ... 6 feeds/day and on the next day or two, I.V. fluids are completely replaced by nasogastric or oral feeding.

+ ***Antibiotic therapy:*** For 10 days. There are 2 choices:
  Combination of - Ampicillin: 200 mg … I.V., every 6 hours.
  - Gentamicin: 20 mg … I.V., every 12 hours.

  OR Cefuroxime: 500 mg … I.V. every 12 hours

± ***Digitalization.***

± ***Mechanical ventilation.***

9. Acute Bronchiolitis

Acute bronchiolitis is a viral interstitial pneumonia commonly occurring between 6 months and 2 years. It is characterized by respiratory distress and expiratory wheezing due to severe bronchiolar obstruction.

Mild cases characterized by expiratory wheezing and minimal or no distress can be managed at home. Oral mucolytics and excess fluid intake are the only required lines of therapy. Oral dexamethasone for few days may be also added in more severe cases to reduce the mucosal oedema. Re-examination after 1-2 days is essential to evaluate the course of illness and to identify severe cases requiring hospital management.

Severe cases characterized by severe respiratory distress and difficult oral intake should be hospitalized for few or several days. Hospital management includes the following aspects:

1. Oxygen therapy: Humidified oxygen can be given by a head box or Venturi oxygen mask with a concentration of 40-60%. Subsequent change in concentration depends on the degree of hypoxemia and the degree of respiratory distress. Repeated measurement of blood gases is important to identify the exceptional extremely severe cases that may necessitate mechanical ventilation.

2. I.V. fluid therapy: Maintenance I.V. fluid therapy for 2-3 days is important to prevent dehydration. Oral feeding can be gradually resumed from the third day with no need for nasogastric feeding.

3. Drug therapy: The role of drugs in management of acute bronchiolitis is doubtful and controversial.

(a) Bronchodilators: Adrenaline, given subcutaneous (0.01 mg/kg/dose), may be useful in reducing mucosal oedema by its alpha-adrenergic effect. Salbutamol, given by nebulization (0.25-0.5 ml of the drug added to 2-3 ml saline), can be given empirically and some infants may benefit from it. Theophylline should be avoided as it increases oxygen requirements.

(b) Corticosteroids: Although their benefit is doubtful, they are widely used in severe critical cases to reduce mucosal oedema especially when the possibility of adenovirus infection is likely. Hydrocortisone is given I.V. in a dose of 5 mg/kg/dose every 6 hours for 2-3 days. Dexamethasone is an alternative.

(c) Antibiotic therapy: It is not routinely indicated. However, it may be used in sick febrile patients with the possibility of superimposed bacterial infection.

4. Mechanical ventilation: Fortunately, the overall prognosis is excellent and more than 95% of cases will show dramatic improvement over 2-3 days. In 1 % of cases, rapid deterioration occurs and mechanical ventilation for few days is lifesaving.

10. Bronchial Asthma

The goal of management in bronchial asthma is to allow the asthmatic child and his family to have as normal lifestyle as possible. Accurate diagnosis of the different aspects of asthma and proper use of the various lines of therapy are important. The strategy of management can be categorized as follow:

1. Symptomatic treatment of the acute asthmatic episodes.
2. Protective treatment to reduce frequency or intensity of symptoms.
3. Avoidance of exposure to triggering stimuli.
4. Patient education and emotional support of the child and his family.

A) Symptomatic treatment of acute episodes

The use of bronchodilators is the mainstay in the management of the acute attack. The choice of the suitable drug or drugs, the route of administration and the place of management depend mainly on the severity of the acute attack and the age of the patient as well. Treatment can be summarized as follow:

- Milk attack: One bronchodilator (at home).
- Moderate attack: Two bronchodilators (at home).
- Severe attack: Two or three parenteral bronchodilators (in hospital).

(a) Home management of mild to moderate attacks

Patients with mild to moderate attacks can be successfully managed at home. Therapy includes the following aspects:

1. Bronchodilators: The choice of the suitable drugs and the route of administration depend on the severity of the attack and the age of the patient:

• **Mild attacks:** The use of **ONE** bronchodilator drug is usually sufficient.

- In children below the age of 6 years, theophylline or a theophylline variant (15-20 mg/kg/day, oral, divided into 3 - 4 doses) or beta 2-agonist as salbutamol or terbutaline (0.1-0.3 mg/kg/day, oral, divided into 3 - 4 doses) are equally effective. Salbutamol can be given by nebulization (0.25-0.5 ml of the drug added to 2-3 ml saline), 3-4 times per day.

- On the other hand, in patients above the age of 6 years, a beta 2-agonist as salbutamol, given by inhalation (aerosol therapy), is preferable and gives an immediate effect. The dose is one puff of the metered aerosol, 3 - 4 times daily. The child should be taught carefully how to use the aerosol and the technique should be repeatedly checked.

• **Moderate attacks:** the simultaneous use of **TWO** bronchodilator drugs (theophylline + beta-2 agonist) is justified. Therapy with bronchodilators should be continued for 3 - 4 days after the child has become wheeze-free. The average

duration of therapy is usually 7 - 10 days. In patients with moderate attacks and previous recent history of severe attack and hospitalization, a short course of oral corticosteroids for 4 - 5 days may be added.

2. Antibiotics: The use of antibiotics is not indicated and will not alter the course of illness. Even in cases precipitated by respiratory infections, the infection is almost always viral in origin. However, antibiotics may be justified in infants or in exceptional cases with high fever where the possibility of superimposed bacterial infection is considerable.

3. Cough medicines: The role of expectorants or cough suppressants in management of the acute attack is minimal. However, some of the preparations of salbutamol or terbutaline contain an expectorant as well (see bronchodilators). In exceptional cases with severe spasmodic cough, a cough suppressant may be used to allay anxiety.

(b) Hospital management of acute severe attacks

- **In emergency depatrment,** an initial management is made with oxygen therapy, subcutaneous adrenaline (0.01 mg/kg/dose) and salbutamol nebulization (0.25-0.5 ml of the drug added to 2-3 ml saline). Both drugs can be repeated after 20 minutes. When salbutamol nebulization is not available, salbutamol inhaler and a "spacer" can be used. Further management will depend on the response:

  - In case of good response, salbutamol nebulization can be given every 2 hours for 2-3 doses and the patient can be then sent home and managed as those with a moderate acute attack (beta 2-agonist + theophylline + steroids).
  - In case of incomplete response, salbutamol nebulization is continued every 20 minutes for 3 doses and steroids (oral or parenteral) should be added. Ipratropium nebulization may be also considered (0.5-1.0 ml of the drug added to 3-4 ml saline). In case of favourable response, treatment can be continued as the group of good response. Failure of these measures necessitates hospitalization.
  - In case of poor response or in deteriorating cases, the patient should be hospitalized.

- **Hospital management** includes the following aspects:

1. Close observation: Heart rate, respiratory rate, degree of retraction, air entry, colour and level of consciousness should be recorded every 1 - 2 hours.

2. Oxygen therapy: Oxygen is essential to correct hypoxemia and to allay anxiety. Moreover, the use of bronchodilators will increase the oxygen requirements. The method of administration depends on the age of the patient. Head box is the most suitable for infants while in older children oxygen mask or nasal prongs can be used. The concentration of 40 - 60% oxygen is usually sufficient. When pulse oximeter is available, oxygen saturation should be kept above 90%. Oxygen should be given continuously and withdrawn gradually. Duration of oxygen therapy in acute severe asthma is usually 1-3 days.

3. I.V. fluid therapy: Maintenance I.V. fluid therapy in the first day or two is important to provide an adequate fluid intake and to prevent dehydration. Oral feeding can be gradually resumed in the second or third day.

4. Drug therapy: Three drugs can be used simultaneously:
- **Nebulized salbutamol** (0.25-0.5 ml of the drug added to 2-3 ml saline) is continued every 1-2 hour.
- **Theophylline** (5 mg/kg/dose, slow I.V., every 6 hours) is also given.
- **Methylprednisolone** (1-2 mg/kg/dose, I.V., every 6 hours).

Treatment is usually continued for 2-3 days after which, the 3 drugs can be replaced by oral preparations for 5-7 days. Parenteral antibiotics are not generally indicated except in infants or when the possibility of superimposed bacterial infection is considerable, as in those with high fever, marked leukocytosis or significantly elevated C-reactive protein.

5. Mechanical ventilation: Fortunately, more than 95% of acute severe attacks respond to the above lines and show significant improvement within 24-48 hours. However, in case of clinical deterioration or when arterial blood gases reveal severe hypoxemia and CO_2 retention, endotracheal intubation and mechanical ventilation are indicated for 1-2 days.

B) Protective treatment or long-term medications

Every asthmatic child should be kept as free from symptoms as possible. Protective drug therapy with **asthma controllers** (mast cell stabilizers and leukotriene modifiers) aims to reduce the frequency or intensity of symptoms, mainly in ***persistent asthma*** where very frequent or daily coughing and wheezing is present between the acute attacks. According to ***NAEPP guidelines***, persistent asthma is classified according to frequency of symptoms into 3 grades:

1. *Mild persistent asthma:* Symptoms are more than 3 times per week.
2. *Moderate persistent asthma:* Daily symptoms and daily use of relievers.
3. *Severe persistent asthma:* Daily symptoms and frequent night symptoms.

The **" 3 strikes rule"** is an easy rule to identify asthmatic children who are in need of controller medications. The asthmatic child is in need of controller therapy if he has any of the following 3 criteria:
1. If he has asthma symptoms more than **3** times per week.
2. If he has night symptoms more than **3** times per month.
3. If he needs to use more than **3** containers of relief inhalers per year.

Recently, asthma controllers can be graded as follows:
* Inhaled corticosteroids are the first-line drugs of choice.
* Long-acting beta 2-agonists and leukotriene modifiers come next.
* Other asthma controllers (long-acting theophylline, ketotifen) are less effective.

The choice of the suitable drug or drugs depends on the severity of persistent asthma and the age of the patient as well:

1. Mild persistent asthma

- Treatment starts with ***low-dose inhaled corticosteriods*** for several weeks. In young children below the age of 6 years where inhalation is difficult, inhalers and a "spacer" can be used.
- As an alternative, oral montelukast (leukotriene modifier) can be used in young children as a first drug.

2. Moderate persistent asthma

- Treatment starts with ***High- dose inhaled corticosteriods*** for several weeks.
- As an alternaive, low-dose inhaled corticosteroids and either long-acting beta 2 agonist or oral montelukast can be used.

3. Severe persistent asthma

- Combined therapy with ***high-dose inhaled corticosteriods and either long-acting beta 2 agonist or oral montelukast*** are usually needed. Recently, inhaled corticosteroids and long-acting beta 2-agonist are available in one preparation (Seretide Diskus). Treatment can continue for several weeks or months.
- Oral steroids may be used in resistant cases.

It is important to remember that ***other asthma controllers*** (as long-acting theophylline and ketotifen) are less effective than the above drugs. However, these drugs have the advantage of availability in cheap oral preparations that can be used in young children or when the patient cannot afford the cost (oral montelukast is the most expensive drug followed by long-acting beta 2-agonists).

C) Avoidance of exposure to triggering stimuli

Some general precautions may be important to asthmatic children:

1. Environmental factors: Exposure to cold, sudden change in temperature or excess humidity should be avoided. Irritant odours, cigarette smoke and car exhaust should be also avoided.

2. House allergens: In children with allergic asthma, house dust and house dust mite are the most common responsible allergens. Control of the house dust with a special attention to the child's bedroom is useful in house dust-allergic children.

3. Respiratory infections: In infants and young children with infective asthma extra measures to avoid respiratory infections are important. Close contact with infected parents, siblings or mates should be avoided.

4. Diet: When a definite history suggests that the acute attacks are related to exposure to a certain food, this particular food should be avoided. On the other hand, the common mistake of preventing all asthmatic children from certain foods as fish, eggs and chocolates should be also avoided.

5. Drugs: Aspirin may precipitate an acute attack in some patients and it is better to be avoided. Propranolol, a beta blocker drug, should be also avoided.

D) Patient education and emotional support

Asthmatic patients should be educated about:

- Nature of the disease and the prognosis.
- How to avoid the triggering stimuli.
- What to do in acute attacks.
- Correct use of inhalers and other delivery systems (as nebulizers).

Most anxieties and worries are related to the following aspects:

1. What are the nature and the outcome of asthma?

Parents should be reassured that the ultimate prognosis of childhood asthma is excellent. With time, attacks will become less frequent and milder. Most children will recover completely and become wheeze-free before adolescence.

2. Could the acute attack lead to suffocation and death?

Parents should realize the importance of early medical consultation for assessment of severity and choice of appropriate therapy. Generally, they should be reassured that death is very unlikely. Even with severe acute attacks, all children with recover within few days of proper hospital management.

3. Does it affect the child's health and development?

Again, parents should be reassured that with proper therapy, the child will have a normal growth and development. Parents should avoid dealing with the child as being fragile and sick. Over concern and overprotection often lead to adverse psychological effects.

4. What are the harmful effects of long-term medications?

With the proper usage of drugs, adverse and harmful effects are almost absent. Even in those receiving a long-term steroid therapy, the inhalation therapy have almost no side effects.

Common mistakes in asthma therapy

1. Use of beta 2 agonists below the age of 18 months: Beta 2 receptors are not well developed below this age, so the therapeutic effect of these drugs is minimal. However, with concomitant use of corticosteroids, the number of beta 2 receptors increases and therapeutic response becomes more evident.

2. Use of corticosteroids as a first line drug in acute severe attacks: Nebulized salbutamol is the most rapid drug. Adrenaline and theophylline are also rapid drugs. Steroids take 4 - 6 hours to show a therapeutic response.

3. Use of antibiotics in acute asthmatic attacks: Antibiotics are not indicated and will not alter the course of illness. Even when respiratory infections are the triggering stimuli, the infection is almost always viral in origin.

4. Use of cough medicines in acute attacks: The therapeutic role of these drugs in asthma is minimal and bronchodilators are the essential line of therapy.

5. Under treatment of persistent asthma: Children with daily coughing and wheezing between attacks are in need of continuous long-term therapy with inhaled corticosteroids alone or combined with other drugs.

6. Use of protective therapy in intermittent asthma: When acute asthmatic attacks are infrequent and only recurring every few weeks or months, protective drug therapy with mast cell stabilizers or leukotriene modifiers is not indicated.

7. Avoidance of certain foods in all asthmatic children: In a small number of asthmatic children when a definite history suggests that acute attacks are precipitated by a certain food, this food should be avoided. Otherwise, asthmatic children should be allowed to eat all foods.

8. Restriction of physical activity: Unfortunately, many asthmatic children are not allowed from parents or teachers to share in games and competitive sports. Such an attitude is harmful to the child's normal development, both physically and socially. Asthmatic children should be encouraged to play and share in sports. Even in children with exercise-induced asthma, the use of salbutamol inhalation before exercise is effective and gives protection for several hours.

Practical examples

1. An infant, one year old (10 kg) with acute mild attack.

RI Minophylline OR Mucophylline syrup (100 mg/5 ml).
1/2 teaspoon (2.5 ml), oral, every 6 hours for 5 - 7 days.

2. A child, 3 years old (15 kg) with acute mild attack.

RI Ventolin OR Farcolin OR Salbuvent syrup (2 mg/5 ml).
1/2 teaspoon (2.5 ml), oral, every 8 hours for 5 - 7 days.

3. A child, 6 years old (20 kg) with acute moderate attack.

RI Etaphylline OR Epicophylline syrup (100 mg/5 ml).
One teaspoon (5 ml), oral, every 6 hours for 5 - 7 days.

RI Bricanyl OR Aironyl OR Osipect syrup (1.5 mg/5 ml).
1/2 teaspoon (2.5 ml), oral, every 8 hours for 5 - 7 days.

4. A child, 6 years old (20 kg) with mild persistent asthma.

RI Flixotide inhaler (50 mcg) OR Flixotide Diskus (50 mcg).
One inhalation, every 12 hours, for several weeks.

5. A child, 6 years old (20 kg) with moderate persistent asthma

RI Flixotide inhaler (125 mcg) OR Flixotide Diskus (100 mcg).
One inhalation, every 12 hours, for several weeks.

± ***RI Singulair OR Kokast OR Clear Air chewable tablets for children (4 mg).***
One tablet every night.

6. A child, 6 years old (20 kg) with severe persistent asthma

- ***Inhaled steroids and oral montelukast***

RI Flixotide inhaler (125 mcg) OR Flixotide Diskus (100 mcg).
One inhalation, every 12 hours, for several weeks.

RI Singulair OR Kokast OR Clear Air chewable tablets for children (4 mg).
One tablet every night.

- ***OR Combined inhaled steroids and long-acting beta 2 agonist***

RI Seretide Diskus (100 mcg).
One inhalation, every 12 hours, for several weeks.

7. A child, 6 years old (20 kg) with moderate persistent asthma. The parents cannot afford the cost of the expensive drugs.

RI Zaditen OR Ketoti OR Zylofen OR Prophallerge syrup (1 mg/5 ml).
1/2 teaspoon (2.5 ml), oral, every 12 hours for several weeks.

RI Quibron SR OR Minophylline SR tablets (300 mg).
1/2 tablet, oral, every 12 hours, for several weeks.

8. A child, 3 years old (15 kg) with acute severe attack, not responding to nebulized salbutamol.

Hospitalization.

Close observation: Degree of respiratory distress, arterial oxygen saturation.

Oxygen therapy: 60% with oxygen mask or nasal prong.

I.V. fluid therapy: 1250 ml/day.

Kadalex: 1000 ml	Over 24 hours
Saline: 250 ml	(17 drops/minute)

(For 1 -2 days then resume oral feeding).

Drug therapy: 1. Salbutamol: 0.25-0.5 ml, nebulization, every 1-2 hour.
2. Theophylline: 75 mg, I.V., over 10 minutes, every 6 hours.
3. Methylprednisolone: 30 mg, I.V., every 6 hours.
(For 2 - 3 days, then replace with oral drugs for another 5 - 7 days).

11. Pulmonary Tuberculosis

Diagnosis of pulmonary tuberculosis is mostly based on suggestive clinical and radiological findings. However, laboratory investigations prior to initiation of therapy are important to confirm the diagnosis. Although ***strongly positive tuberculin test*** and high erythrocyte sedimentation rate are important suggestive findings, these tests may be negative. The ***demonstration of acid-fast bacilli*** in stained smears is the most specific evidence of tuberculosis. In infants and young children, the specimen is collected through gastric lavage, while in older children, bronchial secretions can be obtained through stimulation of coughing. Inability to demonstrate M. tuberculosis either on direct examination or by culture does not rule out the diagnosis, especially when clinical and radiological suspicion are considerable. Recently, ***polymerase chain reaction (PCR)*** is a rapid and sensitive method of identification of the organism.

Unlike all other types of infectious diseases, management of tuberculosis involves months and years of effort. The great majority of children can be managed adequately at home. **Hospitalization** is mainly indicated in young infants or with extensive life-threatening disease as miliary T.B.

The main lines of management are:

1. Chemotherapy with antituberculous drugs: The drug therapy for tuberculosis should be combined (two or three drugs), continuous (given daily) and prolonged (for, at least, 6-9 months). **Isoniazid** (10-15 mg/kg/day) and **rifampicin** (10-20 mg/kg/day) are the two standard oral drugs. After daily administration for 1-2 months, both drugs can be given daily or twice weekly for the remaining 7-8 months with equivalent results. In the twice-weekly regimen, the dose of isoniazid is doubled (20-30 mg/kg/dose) while the dose of rifampicin remains the same (15-20 mg/kg/dose). The addition of **pyrazinamide** during the first two months of therapy reduces the duration of treatment to only 6 months. In case of locally progressive pulmonary disease or miliary T.B., the addition of pyrazinamide during the first 2 months of therapy becomes mandatory and therapy should be continued for at least 9 months.

2. Corticosteroid therapy: It is indicated in endobronchial, pleural or miliary tuberculosis for the first 4-6 weeks of therapy. Prednisone or prednisolone is given orally in a dose of 1 - 2 mg/kg/day.

3. Diet and activity: Adequate nutrition is an important aspect of management. Vitamin and iron supplementation are usually needed especially when nutritional deficiencies are evident. There is no need to restrict activity or to encourage bed rest. The child should attend school activities and should be encouraged to live as normal as possible. Parents should know that the child is not infectious to playmates and family members.

4. Follow-up: Initial clinical and radiological response to therapy does not appear before 2 - 3 weeks of onset of therapy. Clinical evaluation should include the general condition, appetite, activity, chest signs and weight gain. Chest X-ray is important to evaluate the response and can be then repeated every 2 -3 months. Blood picture and E.S.R. may be also checked periodically.

5. Identification of the source of infection: As the infection is mostly acquired from an adult case, all adult family members and other close contacts should be subjected to tuberculin testing and chest X-ray. Treatment of adult cases is important to prevent the spread of the disease to other susceptible contacts. Unvaccinated close contacts to an active case should receive INH prophylaxis for 3 months after which the drug can be discontinued if tuberculin test remains negative. Otherwise, prophylaxis should continue for one year.

Practical examples

1. An infant, 8 months old (7.5 kg) with miliary tuberculosis.

Hospitalization.

\+ *RI Isocid OR inhibex tablets (50 mg).*
Two tablets (crushed), oral (as a single daily dose), for 9-12 month.

RI Rimactane OR Rifamox syrup (100 mg/5 ml).
One and half teaspoon (7.5 ml), oral (as a single daily dose on an empty stomach, one hour before the first morning feed) for 9-12 months.

RI Tebrazid OR Piraldina tablets (500 mg).
Half tablet (crushed), oral, once daily for 2 months.

\+ *RI Hostacortin tablets (5 mg).*
One tablet (crushed), oral, twice daily, for 3 weeks, then half a tablet, twice daily, for another 3 weeks.

\+ *Evaluate the response to therapy after 3 weeks of onset (chest X-ray and E.S.R.).*

2. A child, 6 years old (20 kg) with tuberculosis of tracheobronchial lymph nodes.

RI Isocid forte tablets (200 mg).
One tablet, oral, as a single daily dose, for 6 months.

RI Rimactane OR Rifampicin capsules (150 mg).
Two capsules, oral (as a single daily dose on an empty stomach, one hour before breakfast) for 6 months.

RI Tebrazid OR Piraldina tablets (500 mg).
One and half tablet (crushed), oral, once daily for 2 months.

7

Digestive System

1. Monilial Stomatitis.
2. Herpetic Stomatitis.
3. Recurrent Abdominal Pain.
4. Gastroenteritis.
5. Chronic Diarrhea.
6. Hematemesis.
7. Hepatitis.
8. Acute Hepatic Failure.
9. Chronic Liver Disease.

1. Monilial Stomatitis (Thrush)

Beyond the neonatal period, where monilial stomatitis is common, the condition is mainly seen in malnourished infants or following prolonged antibiotic therapy. It is characterized clinically by a white flaky plaques covering all or part of the to gingiva and oral mucosa. These plaques when removed leave a bright inflamed base. The condition is mildly painful and may cause feeding difficulty.

Management includes the following aspects:

1. Local application of antifungal drugs: The use of any drug should be preceded by trials to remove any large plaques with a moistened cotton-tipped applicator or a wooden tongue depressor. **Nystatin** ***(Mycostatin or Fungistatin oral suspension, 100.000 unit/ml)*** is the most commonly used drug. It is given in a dose of 100.000 unit (1 ml = one dropper) every 6 hours for 7 days. As the drug is not absorbed and acts locally on the oral mucosa and G.I.T., the dose is constant and not relat to age. The drug should be instilled drop by drop to ensure an adequate contact with the inflamed oral mucosa. **Miconazole** ***(Daktarin, or Miconaz or Micazole oral gel, 2%)*** is an alternative and it is given orally in a dose of 30 - 60 mg (1/4 - 1/2 of its own spoon) every 6 hours for 7 days. In severe cases, the two drugs can be used simultaneously.

2. Feeding: As the condition is usually not very painful, feeding can be continued as usual. In severe cases associated with feeding difficulty, the infant can be fed temporarily with a spoon and cup to eliminate the pain and the continued abrasion from nipple feeding.

3. Persistent oral moniliasis: Persistence of monilial infection for more than 10 days in spite of adequate therapy should raise the possibility of immunodeficiency. The condition should also be suspected in frequently recurrent cases. Evaluation of T-cell function by screening and quantitative tests is indicated (see immunodeficiency).

Practical example

An infant, 7 months old (8 kg) with oral moniliasis.

Rl Mycostatin OR Fungistatin oral suspension (100.000 unit/ml).
One ml (one dropper), oral, every 6 hours for 7 days.

OR

Rl Daktarin OR Miconaz OR Micazole oral gel, 2%.
1/4 spoon, oral, every 6 hours for 7 days.

2. Herpetic (Ulcerative) Stomatitis

Acute herpetic gingivostomatitis is the commonest cause of stomatitis in late infancy and early childhood. The condition is most common in children between the age of 1-3 years and is characterized by high fever and painful ulcerations of the tongue and oral mucosa.

Management includes the following aspects:

1. Drug therapy: Treatment is mainly symptomatic and it aims to eliminate the pain until spontaneous recovery occurs in about one week.

(a) Local analgesics: The application of a local analgesic, 10-15 minutes before feeding, several times per day is helpful to alleviate pain and to allow oral-feeding. Available preparations usually contain a local anaesthetic agent ***(Dentocalm, Dentinox, Mundisal or Medijel gel).*** Some preparations can provide a protective thin film over the inflamed mucosa and prevent the direct contact with food ***(Solcoseryl or Orabase dental paste).*** Other preparations are available in the form of a spray that allows easy application ***(BBC spray).*** Any of these preparations can be used.

(b) Analgesics and antipyretics: Systemic analgesics are also required to relieve pain and to control fever, which is around 40°C for 3-5 days. Oral paracetamol (15 mg/kg/dose), ibuprofen (10mg/kg/dose) or mefenamic acid (5 mg/kg/dose) can be used 3 - 4 times per day.

(c) Antibiotics: As the condition is viral in origin, antibiotics will not alter the natural course. They are only useful in case of secondary bacterial infections. Oral erythromycin (50 mg/kg/day) or one of the first-generation cephalosporins as cephalexin, cephradine or cefadroxil (50 mg/kg/day) can be used.

(d) Specific antiviral therapy: Treatment with oral or parenteral acyclovir ***(Zovirax)*** is not recommended for this simple self-limited infection. However, in exceptionally severe cases associated with systemic herpetic infection, the use of this drug may be considered. (See antiviral drugs).

2. Feeding: As the condition is very painful, feeding is usually a real problem. Ice-cold fluids and semisolids are usually more accepted than other foods. Salty or acid foods should be avoided. In infants, temporary shift from bottle to spoon and cup feeding may be necessary.

3. In extremely severe cases, especially in infants, oral feeding may become impossible and fasting dehydration may occur. In these exceptional severe cases, **hospitalization and maintenance I.V. fluid therapy** for few days may be necessary.

3. Recurrent Abdominal Pain

Fortunately, the great majority of children with recurrent abdominal pain do not have any organic disease. However, detailed history, thorough examination and some simple investigations are required to exclude organic causes.

Management of dysfunctional recurrent abdominal pain

1. Reassurance: Parents and the child should be reassured that no major illness is present. The condition is quite common among children and it will subside spontaneously with time and without any therapy.

2. Symptomatic treatment of the pain episode: In most cases, the pain is not severe, not interfering with activity and will subside spontaneously in less than 20 minutes. In severe or prolonged episodes, antispasmodics can be used. Hyoscine butylbromide ***(Buscopan syrup),*** tiemonium ***(Visceralgine syrup)*** or dicycolomine ***(Spasmorest syrup)*** can be used. Several preparations containing a spasmolytic and an analgesic are available in form of suppositories and can be used in severe episodes (as ***Spasmo-pyralgin-M infantile supp).***

3. Chronic simple constipation, if present, may be responsible and should be treated. High residue diet as whole wheat bread, vegetables and fruits may be helpful. Drugs as Lactulose ***(Lactulose or Duphalac syrup)*** or sodium picosulphate ***(Picolax or Normalax drops)*** may be used in cases not responding to simple dietary management (see laxatives).

4. Follow-up: Parents and the child are asked to make a diary of pain episodes, diet, bowel habits and stressful events. During return visits, allow time with the child and the parents separately to uncover hidden stresses. Every effort should be made to normalize the life of the child. At times, children with severe recurrent abdominal pain may turn the doctor to become the patient, as the investigations and management of such cases may injure the self-esteem and affect the behaviour, even of the most self-assured clinicians.

Practical example

A child, 6 years old (20 kg) with recurrent dysfunctional abdominal pain and chronic constipation.

RI Lactulose OR Duphalac OR Sedalac syrup.

Two teaspoons, oral, every night. Dose is adjusted according to the response.

OR RI Picolax OR Normalax Drops.

10-15 drops,oral, every night. Dose is adjusted according to the response.

\+ ***RI Visceralgine OR Spasmorest syrup.***

One and half teaspoon, oral, when needed (severe episode of abdominal pain).

4. Gastroenteritis

Management of acute gastroenteritis in infants and young children requires an **accurate clinical assessment.** Detailed history and thorough examination should be directed to assess the following aspects:

- Severity of diarrhea: Number and volume of motions/day.
- Causative organism: By considering the stool characters.
- Associated symptoms: Severity and duration of fever and vomiting.
- Associated complications: Especially dehydration and electrolyte imbalance.

(For details, see Pediatric Clinical Diagnosis)

Following history and examination, a **clinical decision** should be made regarding the place of management, whether home or hospital.

A) Home management of uncomplicated cases

Most cases of mild to moderate gastroenteritis can be successfully managed at home. Even in severe cases of watery diarrhea, unaccompanied with persistent vomiting or dehydration, initial home management should be tried and is frequently successful. In this case, **re-examination** after 12-24 hours is essential to re-evaluate the condition. In case of clinical deterioration (weight loss or evident dehydration), the patient should be hospitalized. Home management includes the following aspects:

1. Prevention of dehydration.
2. Feeding.
3. Symptomatic treatment (for diarrhea, vomiting and fever).
4. Specific treatment (for bacterial or protozoal infections).
5. Follow-up.

1. Prevention of dehydration: As acute gastroenteritis is a self-limited disease, prevention of dehydration is the most important therapeutic goal. Ice-cold fluids, given in small frequent amounts, are important to compensate for water and electrolyte losses. Weak tea, lemon juice, apple juice, rice water or beverages as Pepsi or Seven-up can be used. In severe cases of watery diarrhea, the **oral rehydration solution** ***(Rehydran or Rehydro-zinc)*** should be used. The contents of the packet are dissolved in 200 ml cooled previously boiled water. The amount needed per day is about 150 ml/kg. Fortunately, the actual amount needed is naturally regulated by the thirst mechanism and the dehydrated patient is always craving for water. Oral rehydration therapy is usually continued for about 24 - 48 hours after which gradual re-feeding should be resumed.

2. Feeding: The necessity for modification of feeding in acute gastroenteritis is mainly related to the severity of the condition and the possible digestive complications especially lactose intolerance and milk allergy.

(a) In mild cases (3-6 motions/day), feeding can be continued as usual with no need for any modification.

(b) In moderate cases (6 -10 motions/day), some modification of feeding may be required. In breast-fed infants, partial or incomplete breast-feeding is recommended for few days where the infant receives either a less number of feeds or receives the breast for shorter periods. In artificially fed infants, a diluted milk formula (1/3 or 1/2 strength) is prescribed for few days with daily gradual increase in strength. In weaned infants or young children, feeding is started with introduction of semisolids as starch pudding, jellies, boiled vegetables (carrots and potatoes) and fruits as banana. Other foods as cereals, minced chicken, yogurt are added gradually.

(c) In severe cases of watery diarrhea (more than 10 motions/day) and after the first 24-48 hours on oral rehydration solution, a more cautious gradual re-feeding is recommended, where the same principles mentioned for moderate cases are applied but with a more gradual schedule. Several commercial ready-made preparations are available for feeding these convalescent infants. Some of these preparations are mainly made of precooked rice ***(Rizini rice, Cerelac rice or Gerber rice),*** while others are containing mainly carrots ***(Bebelac carrot or Camegel).*** These preparations can be given either as separate feeds or one or 2 spoons of any are added to the diluted milk formulas.

(d) If watery diarrhea reappears after initial improvement or becomes worse on re-feeding with milk (re-feeding diarrhea), the possibilities of lactose intolerance and/or milk allergy should be considered. Prescribing a lactose free hypoallergic formula ***(Isomil or Nursoy or Bebelac FL formula)*** for about one week is recommended until regeneration of intestinal mucosa takes place. These formulas have the disadvantage of bad taste and may be rejected by the infant. In this case, another special formula with a better taste ***(Milupa special formula or Galactina special nutrition)*** can be used in either liquid or semi-sold forms. When severe watery diarrhea continues in spite of these formulas, the diagnosis of monosaccharide intolerance is considered. Hospitalization and I.V. fluid therapy for several days may be necessary and total parenteral nutrition is occasionally required.

3. Symptomatic treatment: Control of symptoms especially vomiting is important to prevent fasting dehydration and to allow for replacement of losses induced by the diarrhea. High fever also is harmful as it commonly aggravates the vomiting and increases the likehood of dehydration by excess water losses through the skin and the respiration.

(a) Control of vomiting: The administration of the ice-cold fluids in small amounts is frequently effective. Antiemetic oral drugs as **metoclopramide** (0.5 mg/kg /day) or **domperidone** (1.0 mg/kg/day) can be prescribed and given in 3-5 divided doses, 30 minutes before feeding.

In severe cases, metoclopramide can be given I.M. in two divided doses. Severe persistent vomiting in spite of the above measures is an indication for hospitalization and I.V. fluid therapy.

(b) Control of fever: Excess intake of cold fluids is partially helpful. Administration of oral antipyretics as paracetamol (15 mg/kg/dose) or ibuprofen (10 mg/kg/dose) 3-4 times per day may be required. With high fevers, tepid sponges are also needed. Antipyretic suppositories are contraindicated with severe diarrhea (see antipyretics).

(c) Control of diarrhea: Although a large number of *nonspecific antidiarrheal preparations* are available ***(Enteroquin, Streptoquin or Diamycin suspension)*** and commonly prescribed, the therapeutic value of these drugs is doubtful. Recently, it is recommended by WHO and UNICEF that all children with acute diarrhea in developing countries should receive *oral zinc supplementation* for 10-14 days (10-20 mg/day). Available zinc preparation is ***Aqua Ream Z syrup (15 mg elemental zinc/5 ml)***. There is strong evidence that zinc supplementation to children with diarrhea leads to reduced duration and severity of diarrhea and could prevent deaths. It is important to emphasize that the antimotility drugs as diphenoxylate (Lomotil) or loperamide (Imodium) are absolutely contraindicated in acute gastroenteritis and may be very harmful.

4. Specific treatment: In the majority of cases of acute gastroenteritis, the diarrhea will subside spontaneously within 3 - 7 days without any specific therapy. However, specific treatment is indicated in the following conditions:

(a) Antibiotic therapy: It is indicated when severe bacterial infection is strongly suspected. Persistent high fever and bloody diarrhea are the main indications. Oral drugs as amoxycillin or co-trimoxazole or nifuroxazide (***Antinal or Nifunal suspension***) can be used for 5 days. In severe cases, the I.M. route is preferable and one of the following drugs can be used:

— Ampicillin: 50 - 100 mg/kg/day in 3 - 4 divided doses.
— Cefotaxime: 50 - 100 mg/kg/day in 2 divided doses.
— Gentamicin or tobramycin: 5 mg/kg/day in 2 -3 divided doses.

(b) Antiprotozoal therapy: When stool analysis proves presence of giardiasis or amoebiasis, oral metronidazole ***(Flagyl or Amrizole or Metrozole suspension, 125 mg/5 ml)*** is indicated. For giardiasis, the dose is 25 mg/kg/day for 7 days, while in amoebiasis the dose is 50 mg/kg/day for 10 days. Furazolidone (8 mg/kg/day for 10 days) may be also considered for giardiasis in children.

5. Follow-up: Re-examination and re-evaluation is an integral part of home management of acute gastroenteritis. Patients with severe watery diarrhea should be re-examined and **re-weighed** after 12-24 hours. Clinical deterioration (as evidenced by weight loss, signs of dehydration or severe persistent vomiting) is an indication for hospitalization. In mild to moderate cases, re-examination after 2-4 days is important for re-evaluation and early detection of complications.

B) Hospital management of complicated cases

Hospital management is indicated in the following conditions:

— Clinical deterioration on home management.
— Severe persistent vomiting with mild dehydration.
— Moderate or severe dehydration.
— Presence of other complications as shock, renal failure, metabolic acidosis, convulsions or bleeding.

Hospital management varies according to the severity of the condition:

1. Continuous nasogastric drip: In patients with mild dehydration and history of persistent vomiting, an initial trial of rehydration through the continuous nasogastric drip may be successful. This line of therapy can be made in the emergency room:

- Weigh the patient accurately.
- Give metoclopramide (0.3 mg/kg ... I.M.).
- The oral rehydration solution, placed in a bottle connected to I.V. set, is continuously infused through a nasogastric tube at a rate of 150 ml/kg/day (6 ml/kg/hour or 2 drops/ kg/minute).

In successful cases (no vomiting or weight loss after 6-12 hours), oral rehydration can be started using the cup and spoon (2-3 teaspoons every 10 minutes). Treatment can be then continued at home as those with severe diarrhea.

Persistent vomiting or weight loss in spite of nasogastric drip is an indication for hospitalization and I.V. fluid therapy.

2. I.V. fluid therapy: Patients with moderate or severe dehydration or those with complications should be hospitalized for I.V. fluid therapy. Unsuccessful continuous nasogastric drip is also an indication.

- Initial investigations should include serum electrolytes (Na and K), acid-base status (pH, $PaCO_2$ and HCO_3), blood urea and blood picture.
- Accurate weight and close observation of urine flow are important.
- I.V. fluid therapy is given over 24 hours in 3 successive steps:

(a) Shock therapy (over 1 hour): 10 -20 ml/kg of Ringer's lactate is infused I.V. over 1 hour. This therapy will correct the hypovolemia, renal circulation and the metabolic acidosis. In severe cases of shock, 10 ml/kg of fresh blood or plasma may be given following Ringer's lactate infusion.

(b) Deficit therapy (over 8 hours): The amount given and the solutions used depend on the degree and type of dehydration:

* **Amount:** Mild dehydration: 40 ml/kg.
Moderate dehydration: 80 ml/kg.
Severe dehydration: 120 ml/kg.

(In hypernatremic dehydration, give only 60% of the calculated amount, as full correction may result in cerebral oedema and convulsions).

* **Solutions used:** It depends on the type of dehydration:

• ***In isonatremic dehydration*** (serum sodium is 135 - 145 mEq/liter), glucose 5% and normal saline are mixed in a ratio of 1:1. Potassium chloride solution (15%) is added in amount of 1 ml for each 100 ml of the prepared mixture.

• ***In hyponatremic dehydration*** (serum sodium below 130 mEq/liter), the same mixture used for isonatremic dehydration can be also used. In severe cases with serum sodium below 120 mEq/liter, the hypertonic saline solution 3% should be also used. It is given in a dose of 5 - 10 ml/kg with an infusion rate of 1 ml/minute. Each 1 ml of this hypertonic saline will raise the serum sodium level by about 1 mEq/liter. (For details and accurate dosage, see I.V. fluid therapy).

• ***In hypernatremic dehydration*** (serum sodium above 150 mEq/liter), glucose 5% and normal saline are mixed in a ratio of 4:1 and potassium chloride is added in amount of 1 ml for each 100 ml of the prepared solution. In other words, we give the same mixture used for maintenance therapy. Serious hypernatremia with serum sodium level above 180 mEq/liter may necessitate peritoneal dialysis (see I.V. fluid therapy).

(c) Maintenance therapy (over 15 hours): Solution used is a mixture of glucose 5% and normal saline in a ratio of 4:1. Potassium chloride solution is added in amount of 1 ml for each 100 ml of the mixture. The amount needed for maintenance therapy depends on the body weight:

- For the first 10 kg: 100 ml/kg.
- For each kg from 11 -20 kg: add 50 ml/kg.
- For each kg above 20 kg: add 20 ml/kg.

In case of severe watery diarrhea, the amount should be increased by about 20 - 30% to compensate for the continued losses (see I.V. fluid therapy).

During the next 24 hours, management depends on the clinical condition:

• If the patient is still dehydrated, deficit and maintenance therapy are repeated over the next 24 hours.

• If the patient is fully hydrated but the severe watery diarrhea is continuing, the maintenance therapy plus the expected losses are given over the next 24 hours.

• If the patient is fully hydrated and the diarrhea is improving, gradual oral intake is allowed, where half the maintenance requirements during the next 24 hours are given I.V. and the other half is given orally in the form of oral rehydration solution and other cold fluids. Over the next few days, gradual re-feeding is allowed as those of home management.

3. Treatment of complications: Several complications may occur with cases of severe gastroenteritis and dehydration. Early recognition and proper management of these complications are important.

(a) Septicemia: Parenteral antibiotic therapy is indicated in patients with high persistent fever, especially when associated with cold extremities and mottled

skin (septic shock). Polymorphonuclear leukocytosis and elevated C-reactive protein are confirmatory findings of severe bacterial infection. Ampicillin (100 mg/kg/day) or amoxycillin (100 mg/kg/day) is given I.V. in 4 divided doses every 6 hours. One of the aminoglycosides as gentamicin or tobramycin (5-7 mg/kg/day, I.V. in 2 - 3 divided doses) may be added in severe cases. Therapy is continued for, at least, 5 days.

(b) Renal failure: Severe gastroenteritis and dehydration is the commonest cause of acute renal failure in infants. The condition should be suspected if the patient did not pass urine after completing the initial shock therapy with Ringer's lactate solution. The deficit therapy is then given without adding the potassium chloride solution. Failure to pass urine within 4 hours of initiation of deficit therapy is an indication to evaluate the renal function (blood urea and creatinine) and to try induction of diuresis by drugs (see I.V. fluid therapy and acute renal failure).

(c) Metabolic acidosis: It is a common complication of severe gastro-enteritis and dehydration. Mild to moderate cases are usually corrected by the initial shock therapy with Ringer's lactate solution. Severe persistent acidosis (pH below 7.2 and HCO_3 below 10 mEq/liter) after Ringer's lactate therapy is an indication for correction with sodium bicarbonate. Practical empirical dosage is 4 ml/kg/dose of the 5% solution (For dosage and details, see I.V. fluid therapy).

(d) Hypokalemia: Severe hypokalemia (potassium level below 2.5 mEq /liter) cannot be corrected over the first 24 hours because the concentration of potassium in any solution should not exceed 35 - 40 mEq/liter. Partial treatment of hypokalemia can be made by increasing potassium concentration in the deficit and maintenance solution to 35-40 mEq/liter. Subsequent correction can be made over the next few days with oral potassium therapy (see I.V. fluid therapy and mineral therapy).

(e) Convulsions: Convulsions that may occur with gastroenteritis and dehydration is mostly NOT due to C.N.S. infection. Symptomatic urgent control is made by I.V. diazepam (0.5 mg/kg). Treatment of the cause is the main therapy. High fever (febrile convulsions), shigellosis, salmonellosis (toxic convulsions), hypocalcemia or hypernatremia (metabolic convulsions) are the main causes. Convulsions with bleeding should suggest intracranial hemorrhage due to severe DIC (see I.V. fluid therapy and mineral therapy).

(f) Bleeding: Due to hypoprothrombinemia or DIC.

- Hypoprothrombinemia may occur due to vitamin K deficiency in cases with prolonged fasting. Treatment is made by vitamin K_1 injection (5 - 10 mg, I.V.).
- Successful management of DIC depends on the prompt control of the precipitating factors, mainly shock, acidosis and septicemia. Platelet and fresh frozen plasma transfusion may be considered. Exchange transfusion, if possible, may be useful.

Practical examples

1. An infant, 8 months old (8 kg) with mild enteritis. No fever or vomiting. Breast-fed and partially weaned.

- No treatment. Continue the same feeding.
- Re-examination after 3 - 4 days.

2. An infant, 10 months old (10 kg) with moderate gastro-enteritis, with mild vomiting and no fever. Weaned.

RI Primperan drops (0.1 mg/drop).
10 drops, half an hour before feeding, 4 - 5 times/day for 1 - 2 days.
RI Diakan OR Enteroquin OR Streptoquin suspension.
One teaspoon, 3 times per day, for 3 - 4 days.
RI Aqua Ream Z syrup (15 mg elemental zinc/5 ml).
One teaspoon, per day, for 10-14 days.
\+ Re-examination after 2 - 3 days.

3. An infant, 9 months old (8 kg) with severe watery diarrhea. No fever, vomiting or dehydration.

RI Rehydran OR Rehydro-zinc packets.
One packet + 200 ml cooled previously boiled water, 5 - 6 packets per day.
\+ Re-examination after 24 hours.

4. An infant, 10 months old (8 kg) with severe watery diarrhea, high fever (39.8°C) and moderate isonatremic dehydration.

Hospitalization.
\+ ***Investigations*** (CBC, CRP, serum electrolytes and blood gases).
\+ ***I. V. therapy:***

(a) Shock therapy: 160 ml Ringer's lactate over one hour (53 drops/minute).

(b) Deficit therapy:

320 ml kadalex 320 ml saline	over 8 hours. (26 drops/minute)

(c) Maintenance therapy + expected continued losses:

800 ml kadalex 200 ml saline	over 15 hours (22 drops/minute)

\+ ***Antibiotic therapy:*** Ampicillin: 200 mg, I.V., every 6 hours.
\+ Re-evaluate after the first 24 hours.

5. A child, 2 years old (12 kg) with moderate bloody diarrhea and high fever (? shigella). No vomiting or dehydration.

RI Sutrim OR Chemotrim OR Septazole suspension.
One teaspoon, oral, every 12 hours, for 5 days.
RI Enteroquin compound OR Diamycin OR Streptoquin suspension.
One teaspoon, oral, 4 times daily for 3 - 5 days.
\+ ***Soft diet for 2 days.***
\+ Re-examination after 4-5 days.

5. Chronic Diarrhea

Diarrhea continuing for more than 2-3 weeks is a real challenge to the treating physician. Detailed history, thorough examination and some investigations are all necessary. Family history and history of weight loss are important. Examination should include inspection of the stool, growth assessment and chest examination. Chronic diarrhea in conjunction with chronic chest disease should suggest cystic fibrosis, tuberculosis or immunoglobulin A deficiency. Fortunately, and in spite of the large number of causes, most cases in infants and young children are caused by few conditions. Chronic giardiasis, post-enteritis malabsorption, celiac disease and chronic non-specific diarrhea are by far the commonest causes. (See Pediatric clinical diagnosis).

Initial simple investigations

1. Stool analysis: It is useful for detection of:

- Protozoal infection: Giardiasis or amoebiasis (repeated analysis is important).
- Parasitic infestation: Bilharziasis in endemic areas.
- Disaccharide intolerance: low pH (acidic) with high sugar content (positive for reducing substance).
- Fat malabsorption (steatorrhea): Microscopic examination for fat cells is a good screening test.

2. Blood picture: It is useful for detection of:

- Anemia: Iron deficiency and folic acid deficiency anemia are common with chronic malabsorption.
- Acanthocytes: Abetalipoproteinemia (acanthocytosis).

Other investigations are individualized and depend on the clinical suspicion. Tuberculin test and chest X-ray (tuberculosis), sweat chloride test (cystic fibrosis), immunoglobulin levels (immunodeficiency) and per-oral intestinal mucosal biopsy (celiac disease) may be indicated in selected cases.

Management of chronic diarrhea is either specific or nonspecific:

A) Specific therapy

It is indicated in diagnosed conditions and when specific therapy is available:

1. Chronic infections: The main causes are:

- Giardiasis: Metronidazole (25 mg/kg/day, oral for 7 days).
- Amoebiasis: Metronidazole (50 mg/kg/day, oral for 10 days).
- Bilharziasis: Praziquentel (50 mg/kg, oral, single dose).
- Tuberculosis: See antituberculous drugs.

2. Post-enteritis malabsorption: It is a common transient complication of severe gastroenteritis characterized by watery diarrhea, which appears on re-feeding with milk. Sugar intolerance and/or milk allergy are the main causes. Prescribing a **Hypo-allergic lactose-free formula** ***(Isomil or Nursoy)*** for a week or two is indicated until regeneration of the injured intestinal mucosa takes place. In exceptionally severe cases of monosaccharide glucose-galactose intolerance, all formulas are ineffective and total parenteral nutrition is indicated till intestinal regeneration takes place. (See nutrition).

3. Fat malabsorption: Therapy of depends on the diagnosis:

(a) Bilary atresia: See neonatal jaundice.

(b) Cystic fibrosis: Oral intake of the deficient **pancreatic enzymes** immediately before meals is the main therapy. Infants and young children can take a syrup form ***(Digestin or Siropostine-S syrup)*** in a dose of 1 - 2 teaspoon, 3 times daily before meals, while older children or adolescents can take the tablet form ***(Zymogen forte or Cotazym forte tablets)*** in a dose of one tablet, 3 times daily, before meals. Treatment is life long.

(c) Celiac disease (Gluten induced enteropathy): Diarrhea usually starts at the age of 6 - 12 months with the onset of introduction of foods containing wheat or rye to the infant's diet (cereals and bread). The stool is bulky, greasy, frothy and offensive. A useful therapeutic test is the clinical response within a week to a **gluten-free diet.** All foods containing wheat or rye (containing gluten) should be completely eliminated from the infant's diet. Foods to be avoided are: all wheat and rye cereals, macaroni, noodles, all breads, cakes, puddings and cookies. Foods allowed (gluten-free) are: milk, cheese, eggs, meat, chicken, vegetables and fruits. Some commercial precooked cereals are gluten-free and can be used. It is important to remember that puffed rice and cornflakes are gluten-free. Patients responding to gluten-free diet should continue on that diet up to the age of 2 years. At this time, re-introduction of foods containing gluten is tried (challenge test). If symptoms recur, per-oral intestinal mucosal biopsy is indicated. In proved celiac disease, treatment with gluten-free diet is life-long.

(d) Acrodermatitis enteropathica: Diarrhea and skin lesions respond dramatically to oral **zinc therapy** in a dose of 50 -150 mg/day. Available preparations are ***Vitazinc capsules (25 mg) and Vital-zinc tablets (22.5 mg).*** Therapeutic response can be also achieved by one of preparations containing diiodohydroxyquin ***(Enteroquin suspension or Diakan suspension).***

B) Nonspecific therapy

It is indicated in conditions where specific therapy is not available or when accurate diagnosis cannot be made (chronic nonspecific diarrhea). The aim of therapy is to achieve a symptomatic control of diarrhea and to supplement the deficient vitamins (fat soluble) and minerals (iron and calcium).

1. Symptomatic control of diarrhea: Judicious use of antimotility drugs may be considered. Diphenoxylate ***(Lomotil)*** may be used in a dose of 0.5 mg/kg/day, oral, in divided doses. Loperamide ***(Loperazine)*** is an alternative and can be given in a dose of 0.2 mg/kg/day, oral, in divided doses. Overdosage of these drugs is serious and may lead to paralytic ileus, respiratory and CNS depression (see antidiarrheal drugs).

2. Supplementation of fat-soluble vitamins: Vitamin deficiencies of A, D and E are common with chronic diarrheas, especially with cases of fat malabsorption (steatorrhea). Oral supplementation of these vitamins in large doses is important. Several preparations are available and can be used (see vitamin therapy).

3. Supplementation of zinc: Recently, it is recommended by WHO and UNICEF that all children with acute diarrhea in developing countries should receive *oral zinc supplementation* for 10-14 days (10-20 mg/day). Available preparation is ***Aqua Ream Z syrup (15 mg elemental zinc/5 ml)***. There is strong evidence that zinc supplementation to children with diarrhea leads to reduced duration and severity of diarrhea and could prevent deaths.

4. Supplementation of iron and calcium: Iron and calcium deficiencies are common with chronic diarrheas. Oral supplementation is indicated in proved deficiency. (See mineral therapy).

Practical examples

1. An infant, 11 months old (10 kg), with mild to moderate watery diarrhea for 3 weeks. Stool examination revealed giardia lamblia infection.

RI Flagyl OR Amrizole OR Metrozole suspension (125 mg/5 ml).
One teaspoon, oral, twice daily, for 7 days.

\+ ***Repeat stool analysis after termination of therapy.***

2. An infant, 10 months old (8 kg), with chronic diarrhea for 2 months. Clinical examination and investigations failed to reveal a specific cause. Therapeutic test on gluten-free diet for 10 days was ineffective (chronic nonspecific diarrhea).

RI Lomotil liquid (2.5 mg/5ml).
One taespoon, oral, twice daily.
OR
RI Loperazin OR Lopodium syrup (1 mg/5 ml).
One taespoon, oral, twice daily.

And
RI Aqua Ream Z syrup (15 mg elemental zinc/5 ml).
One taespoon, oral, once daily for 10-14 days.

6. Hematemesis

The main causes of hematemesis in children are acute gastric ulceration and esophageal varices. Swallowed blood due to oral or nasal causes should be routinely excluded (see Pediatric Clinical Diagnosis).

1. Acute gastric ulceration (Stress ulcers)

Acute gastric ulceration is commonly seen in critically sick patients. Severe gastroenteritis and dehydration, septicemia, shock, burns and head trauma are the main causes. Coffee ground vomiting is the only symptom and no bleeding from other areas. Disseminated intravascular coagulation (DIC) should be excluded.

Treatment includes the following:

1. Gastric lavage: Repeated gastric lavage with ice-cold saline is useful to cause vasoconstriction of gastric mucosa.

2. Drugs: Administration of an **antacid** ***(Epicogel or Mucogel syrup)*** in a dose of 5-10 ml, 3-4 times/day, oral is important to neutralize the gastric acidity. **Cimetidine** ***(Tagamet syrup, 200 mg/5 ml)*** may be also given in a dose of 40 mg/kg/day, oral, in divided doses. The drug is also available in parenteral form to be given I.M. or slow I.V. every 4-6 hours ***(Tagamet amp., 200 mg/2 ml).*** The condition usually subsides within 1-2 days.

2. Esophageal varices

Management of esophageal varices is both medical and surgical:

1. Medical treatment: It includes the emergency measures necessary to control the bleeding episode:
- Urgent whole blood transfusion (20 ml/kg) to compensate for the blood loss. Infuse Ringer's lactate until the blood becomes available.
- Insert a nasogastric tube and aspirate the blood repeatedly to know the amount and rate of blood loss.
- Fortunately, most cases in children respond to the above measures and bleeding stops spontaneously. If the bleeding persists, tamponade, using a Sengstaken-Blakemore tube may be required.

2. Surgical treatment: Endoscopic injection of sclerosing material into the esophageal dilated veins may be tried. Surgical shunting operation is usually required to control portal hypertension.

7. Hepatitis

Once the clinical diagnosis of hepatitis has been made, **simple investigations** as serum bilirubin level (total, conjugated and unconjugated), and serum transaminases (SGOT and SGPT) are indicated to confirm the diagnosis and to provide a base data for follow-up. Other tests to identify the responsible virus **(hepatitis markers)** are available and can be made. These tests are:

- **Antihepatitis A virus antibodies:** Anti-HAV IgM and anti-HAV IgG.
- **Hepatitis B virus antigens and antibodies:** Hepatitis B surface antigen (HBsAg), hepatitis B surface antibodies (anti-HBs) and hepatitis B core antibodies (anti-HBc IgG and anti-HBc IgM).
- **Antihepatitis C virus antibodies** (because no detectable antigens have been found in blood). Recently, polymerase chain reaction (PCR) can assay the viral RNA but the test is expensive and time consuming.

It is important to remember that hepatitis can be occasionally caused by other infectious agents. Cytomegalovirus, brucellosis or malaria can produce hepatitis. In recurrent or chronic hepatitis, Wilson disease should be excluded.

A) Management of uncomplicated hepatitis

Fortunately, most cases of viral hepatitis in children recover spontaneously within 2 - 4 weeks without any therapy. Management includes the following:

1. Bed rest: It is usually indicated during the acute phase of the disease (first 1 - 2 weeks). Activity can be gradually resumed with the onset of decline of bilirubin and transaminase levels.

2. Diet: Protein and fat restriction during the first week is required, especially in presence of anorexia, vomiting or abdominal pain. During this period, Carbohydrates, vegetables and fruits are allowed. Once the appetite improves, proteins and fats are gradually allowed.

3. Drugs: All drugs should be avoided since many of them are metabolized in the liver. Fever, vomiting and abdominal pain usually subside spontaneously within 2-5 days. Antipyretics and antiemetics should be avoided. In severe cases of anorexia and vomiting, hospitalization and intravenous fluid therapy for few days may be necessary to prevent fasting dehydration. Corticosteroids are not indicated for uncomplicated hepatitis and may even be harmful. Antacids, digestants or vitamins are not required.

4. Follow-up: Measurements of serum bilirubin and transaminases should be repeated every 7 - 10 days until levels return to normal values.

5. Health precautions: Parents should know that the child with hepatitis A is infectious, through stool, for about one week after the onset of jaundice. During period, great care should be taken while dealing with the stool or with fecal contaminated materials. Hand washing and the use of a disinfectant are very important. Household contacts may receive immunoglobulin injection (0.5 - 1.0 ml, I.M.) to prevent hepatitis. Patients with hepatitis B are infectious through blood, needles or instruments contaminated with blood. Sampling for investigations should be carefully made to avoid infection. Household contacts can be protected by receiving hepatitis B immunoglobulin (1.5-3.0 ml, I.M.).

B) Management of complications

Although most patients recover spontaneously over weeks, some of them may develop serious acute or chronic complications

1. Acute fulminant hepatitis: In some patients, especially with hepatitis B virus infection, the course is rapidly progressing with deep jaundice, persistence of fever, vomiting and abdominal pain. Oedema, bleeding and disturbed consciousness are manifestations of frank acute hepatic failure. These patients should be hospitalized and managed as those with acute hepatic failure (see acute hepatic failure).

2. Chronic hepatitis: The term chronic hepatitis is limited to cases with evidence of continuing hepatic inflammation for 6 months or more.

- In **chronic persistent hepatitis,** symptoms are minimal and mild elevation of serum bilirubin and enzymes are the only laboratory findings. Prognosis is good and no treatment is required.

- In **chronic active hepatitis,** which may occur with hepatitis C or B virus infection, symptoms are more evident and include fatigue, anorexia, jaundice and may be arthritis. Moderate elevation of serum bilirubin and transaminases is usually present. Serum immunoglobulin levels are usually markedly elevated. Positive Coombs test and antinuclear antibodies may be detected. Definitive diagnosis is made by liver biopsy. Over 75% of cases respond to therapy with corticosteroids. Prednisone is given in a dose of 1-2 mg/kg/day and is continued till transaminase levels return to values twice the normal levels. The dose is then reduced gradually over 4-6 weeks until a maintenance dose of less than 20 mg/day is achieved.

3. Aplastic anaemia: It may develop several weeks after recovery. It has a poor prognosis (see hematology).

8. Acute Hepatic Failure

Although uncommon, acute hepatic failure is a catastrophic event with mortality rate approximating 70%. Unfortunately, there is no specific therapy that can promote hepatic regeneration, so the treatment is mainly supportive and aims to preserve life, to prevent and to deal with complications until natural recovery takes place. Repeated clinical and laboratory evaluation is of great value for planning of successful therapy.

A) Clinical evaluation

A flow sheet recording all relevant clinical aspects every 2 - 4 hours is essential. Recording should include:

- Level of consciousness, tremors, convulsions or rigidity.
- Vital signs: H.R., R.R., B.P. and temperature.
- Evidence of bleeding: Site and amount.
- Urinary output: Use collecting urine bag or urinary catheter.
- Evidence of fluid retention: Oedema or ascites.
- Evidence of associated infections.

B) Laboratory evaluation

Repeated measurement of the following parameters is important:

- Liver functions: Serum bilirubin, transaminases (SGOT, SGPT) and serum albumin.
- Coagulation studies: Prothrombin time and partial thromboplastin time.
- Blood ammonia level (normal value is 40 - 80 mcg/100 ml).
- Serum electrolytes: Na, K (important), Ca and Mg.
- Evaluation of renal function: Blood urea and creatinine levels.

C) Management

Management of acute hepatic failure includes the following aspects:

1. Water, electrolyte and nutritional support: In patients with altered consciousness or in those with gastrointestinal bleeding, **I.V. fluid therapy** is indicated. A solution made of glucose 10% and saline in a ratio of 4: 1 is initially used in an amount equal to the daily requirements. However, the calculated amount should be reduced by 30% in presence of fluid retention or cerebral oedema. As hypokalemia is common, **potassium** chloride solution 15% is added to the I.V. fluids in amount of 1.75 ml for each 100 ml of the glucose saline mixture (35 mEq/liter). Subsequent changes in Na or K contents will depend on serum levels. Daily **calcium** and **magnesium** supplementation is important if I.V. fluid therapy is continuing for several days. **Water soluble vitamins** may be added to the I.V. fluids ***(Parenterovite amp.)*** or given through

a nasogastric tube. **Salt free albumin 20%** (5 ml/kg ... I.V.) is indicated in severe hypoalbuminemia. In recovering patients and after control of G.I.T. bleeding, **nasogastric feeding** or **oral feeding** can be gradually resumed. Diet is initially made of carbohydrates. Proteins and fats are gradually added.

2. Measures to decrease blood ammonia level: As high ammonia level is responsible for hepatic encephalopathy, reduction of blood ammonia level is important. Proteins are completely eliminated from the diet. **Neomycin** ***(Neomycin syrup, 125 mg/5 ml)*** is given through a nasogastric tube in a dose of 50 - 100 mg/kg/day in 4 divided doses (every 6 hours) to sterilize the bowel. **Lactulose** ***(Lactulax or Laxolac)*** is also used to decrease microbial ammonia production. It is given orally or with a nasogastric tube in a dose of 10 ml every 6 hours. The dose should be adjusted to produce several loose motions per day.

3. Control of bleeding: The blood in the stomach should be aspirated through a nasogastric tube and an **antacid** (Aluminium hydroxide gel) is given in a dose of 10 ml, 3 - 4 times/day. **Vitamin K1*(Konakion)*** is given I.V. in a dose of 5 - 10 mg daily. **Fresh frozen plasma** is given in an amount of 10 ml/kg, I.V. **Fresh whole blood transfusion** (20 ml/kg) is indicated in severe hemorrhage to compensate for blood loss. **Lactulose enema** (one volume lactulose and 3 volumes water) may be used to clean the bowel.

4. Control of infections: Several infections may occur and are commonly the cause of death. Ampicillin (100 mg/kg/day, I.V. in 4 divided doses) is given as a prophylaxis. Septicemia, pneumonia, peritonitis or urinary tract infections should be vigorously treated with the appropriate antibiotics and according to the results of cultures.

5. Treatment of cerebral edema: It depends on severity of the condition:

- **Mild cases:** Fluid restriction to 70% of requirements and oxygen therapy (40 - 50%). Oxygen should be continued until the patient regains consciousness.

- **Moderate cases:** Osmotic diuresis with mannitol 20% (5 - 10 ml/kg, I.V. over 30 minutes, every 6 hours for 2 days). Dexamethasone may be also used in a dose of 0.5 mg/kg, I.V. every 12 hours for 2 days.

- **Severe cases:** Mechanical ventilation and hyperventilation to keep $PaCO_2$ around 30 mmHg.

6. Treatment of fluid retention and ascites: Fluid restriction is the initial step. Diuretics are preferably to be avoided, but if necessary, spironolactone (5 mg/kg/day in 2 divided doses) is preferable as it preserves potassium. Abdominal paracenthesis for ascites is only indicated when it is causing mechanical compression and dyspnea.

7. Treatment of hepatorenal failure: See acute renal failure.

9. Chronic Liver Disease

Infants or children with chronic liver diseases are in need of periodic clinical and laboratory evaluation:

Clinical evaluation is mainly directed to features of chronic liver cell failure (jaundice, oedema, ascites and bleeding) and manifestations of portal hypertension (splenomegaly, esophageal varices and dilated abdominal wall veins).

Laboratory evaluation of hepatic functions is made by measurements of serum bilirubin, serum albumin and coagulation mechanism especially prothrombin time. Enzymes released by damaged hepatocytes as SGOT and SGPT may be also measured.

On the basis of clinical and laboratory evaluation, patients with chronic liver disease can be classified as:

(a) Compensated liver disease where clinical or laboratory evidence of chronic liver cell failure are absent.

(b) Decompensated liver disease where clinical and laboratory evidence of chronic liver cell failure are present. Prognosis depends on the severity of clinical and laboratory abnormalities. Patients with massive ascites, deep jaundice, very low albumin and prolonged prothrombin time have a poor prognosis.

Management of chronic liver diseases includes the following aspects:

1. Nonspecific management: It aims to preserve hepatic functions and maintain the well being of the patient. Good diet, moderation of activity, vitamin supplementation, correction of anemia, treatment of esophageal varices, control of infections are the main aspects of management. Avoidance of factors that may aggravate the condition is also important. Constipation, gastrointestinal hemorrhage, excessive use of diuretics or other hepatotoxic drugs should be avoided.

2. Specific management: there are only two hepatic diseases in which specific therapy is available; chronic active hepatitis and Wilson disease. **Chronic active hepatitis** is treated with corticosteroids. In **Wilson disease**, foods with high copper content as liver, nuts and chocolate should be avoided. *D-penicillamine* is the mainly used copper-chelating agent. It is given orally in a dose of 500 mg/day, in 2 divided doses ***(Artamine capsules, 250 mg).*** Treatment is life long. Asymptomatic siblings should also receive treatment.

3. Liver transplantation: In patients with progressive chronic liver cell failure, liver transplantation is the dramatic treatment of choice.

8

Urinary System

1. Glomerulonephritis.
2. Nephrotic Syndrome.
3. Urinary Tract Infection.
4. Nocturnal Enuresis.
5. Acute Renal Failure.
6. Chronic Renal Failure.

1. Glomerulonephritis

Most cases of poststreptococcal glomerulonephritis can be managed at home. More than 95% of cases will recover completely within few weeks and even without therapy. Hospitalization is only indicated in occasional severe cases complicated with severe hypertension, marked vascular congestion or severe acute renal failure.

Management includes the following aspects:

A) General measures

1. Bed rest: It is only indicated during the oliguric phase of illness (first week). After diuresis, activity has no harmful effects on healing.

2. Diet: High carbohydrate diet is recommended to provide adequate calories. Protein and salt restriction are indicated during the oliguric phase and in presence of complications especially severe hypertension and marked vascular congestion.

3. Fluid balance: During the oliguric phase of illness, measurement of the daily urinary output is important. The total daily fluid intake should equal the urinary output of the previous day plus the insensible water losses, which is about 300 ml/day.

e.g. If urinary output of previous day is 250 ml.
So, the total fluid intake of today will be 250 + 300 = 550 ml.

B) Specific measures

1. Eradication of streptococcal infection: An oral course of phenoxy-methyl penicillin ***(Ospen suspension)*** or erythromycin for 10 days is generally recommended to minimize the spread of the nephritogenic organisms.

2. Control of hypertension: Hypertension is present in 70% of cases and blood pressure usually falls to normal by the end of the first week. Treatment with drugs is indicated when diastolic pressure exceeds 95 mmHg. In most cases, one of the oral antihypertensive drugs is usually sufficient. The choices are:

- Captopril ***(Capoten tablets, 25 mg):*** 0.5-1.0 mg/kg/day (divided into 3 doses).
- Hydralazine ***(Apresoline tablets, 50 mg):*** 1-2 mg/kg/day (divided into 3 doses).
- Nifedipine ***(Adalat capsules, 10 mg):*** 0.25-0.5 mg/kg/dose (every 8 hours).

3. Control of edema: In most cases, edema subsides spontaneously by the end of the first week and with the onset of diuresis. Fluid restriction and salt restriction during the first week are usually sufficient. In more severe cases, negative fluid balance is required where the total daily intake should be less than the calculated amount. Diuretics as furosemide may be used to induce diuresis.

C) Treatment of complications

The main complications of poststreptococcal glomerulonephritis are hypertensive crisis, heart failure and renal failure.

1. Hypertensive crisis: In some patients, hypertension is severe and may lead to hypertensive encephalopathy or hypertensive heart failure. One or more of the following drugs can be used:

- **Nifedipine** (0.2-0.5 mg/kg/dose, oral) is very effective with rapid onset of action. The contents of gelatin capsule ***(Epilat capsule, 10 mg)*** may be placed sublingually for immediate effect.
- **Furosemide** (2 mg/kg/dose, I.V) can be also given ***(Lasix amp., 20 mg).***
- **Methyl dopa** (5-10 mg/kg/dose, I.V) is an alternative ***(Aldomet amp., 250 mg).***
- **Hydralazine** (0.2-0.5 mg/kg/dose, I.V) is effective in 30 minutes with duration of action of 30-60 minutes ***(Apresoline amp., 20 mg).***

2. Heart failure: It may occur in severe cases due to severe hypertension (afterload failure), severe vascular congestion (preload failure) or myocardial ischaemia (contractility failure). Fluid restriction and prompt control of hypertension are of prime importance. A trial to induce diuresis by I.V. furosemide in a dose of 2 mg/kg is recommended. In more severe cases, cautious digitalization or dopamine continuous infusion may be considered (see inotropic drugs and acute congestive heart failure).

3. Renal failure: Acute poststreptococcal glomerulonephritis is the commonest glomerular cause of acute renal failure in children. In most cases, renal failure is mild and transient. In occasional severe cases, the manifestations of acute renal failure become evident with severe oliguria or anuria, marked vascular congestion, acidotic breathing and altered consciousness (see acute renal failure).

Follow- up

Gross urinary changes usually last for about one week. However, microscopic hematuria may persist for several weeks. Persistent hypertension or gross urinary changes is a bad prognostic sign as it denotes an evidence of progression to chronic renal failure. Evaluation of renal function is indicated.

2. Nephrotic Syndrome

Most cases of nephrotic syndrome can be successfully managed at home. Hospitalization is only indicated in the first episode for proper control or in subsequent relapses with marked edema. Bed rest is not indicated and children with mild edema can even attend school activities. Management of nephrotic syndrome includes the following aspects:

1. Induction and maintenance of remission by corticosteroids:

- Induction of remission is made by oral ***daily therapy*** with prednisone or prednisolone in a dose of 2 mg/kg/day, divided into 3 - 4 doses. Daily therapy is continued for one week after the urine has become free of proteinuria. Therapeutic response usually occurs in 2-4 weeks. Absence of response after one month of daily therapy is an indication for renal biopsy.
- Maintenance of remission is then made by the ***alternate-day therapy*** where the daily dose is given as a single dose every other morning with breakfast for a period of 3 - 6 months. In case of relapse during or after maintenance therapy, treatment is resumed with the daily therapy to induce remission followed by alternate-day therapy for a more prolonged period (6 - 12 months).
- In children with frequent relapses, cyclophosphamide is indicated to prolong the duration of remission. It is given orally in a dose of 2 - 3 mg/kg/day as a single dose for a period of 8 weeks. Alternate-day therapy with prednisone is also continued during the course of cyclophosphamide therapy. Leukocytic count is monitored weekly and cyclophosphamide is discontinued if count falls below 5000/cmm.

2. Control of edema: With mild edema, corticosteroid therapy and salt-free diet are usually sufficient. In moderate cases, a diuretic as **furosemide** is given orally in a dose of 2 mg/kg/day. Salt free diet and fluid restriction for a week may be also required. Oral potassium supplementation in a dose of 1-2 mEq/kg/day is needed to prevent hypokalemia. In case of marked edema, associated with severe hypoalbuminemia, a **salt-free albumin** (20% solution) is given I.V. in a dose of 5 ml/kg over a period of 2 hours followed by I.V. furosemide (2 mg/kg), then treatment is continued with the oral diuretic therapy.

3. Diet and fluid intake: Diet should be high in proteins to compensate for the protein loss in urine. Salt-free diet is also indicated for one or two weeks until oedema subsides. Fluid restriction is only indicated in moderate or severe cases of oedema.

4. Control of infections: Patients with nephrotic syndrome are immunologically compromized and are susceptible to several infections. Some nephrologists recommend the administration of daily oral penicillin as prophylaxis against pneumococcal infections. Skin infections and bedsores of

the oedematous skin should be avoided by the proper nursing care. Nephrotic syndrome is afebrile disease, so, presence of fever is usually a sign of associated infection. Blood culture is indicated in case of suspicion and infections should be vigorously managed with the appropriate antibiotic therapy.

5. Follow-up: In hospitalized patients, the weight, urinary output, blood pressure and temperature should be recorded daily. Urinary proteins per 24 hours and serum proteins should be measured weekly until the induction of remission is achieved. During maintenance therapy, urinary proteins may be measured every month.

Prognosis

Fortunately, more than 90% of cases will respond to steroid therapy. Although about 70% of cases will have one or 2 relapses, the ultimate prognosis is good with no deterioration of renal functions. In less than 10% of cases, nephrotic syndrome is caused by chronic glomerular disease. In this group, the response to steroids is poor and the condition will eventually progress to chronic renal failure.

Practical examples

1. **A child, 5 years old (20 kg) with the first episode of nephrotic syndrome. Edema is moderate.**

Hospitalization.

+ *High protein, salt-free diet and fluid restriction.*
+ *Daily recording of weight, urinary output, blood pressure and temperature.*

+ *RI Hostacortin OR Hostacortin H tablets (5 mg).*
  2 tablets … oral … 4 times daily for one week after control of proteinuria (usually 3 - 4 weeks) then, 8 tablets ... as a single oral dose, every other day (in the morning with breakfast) for 6 months.

+ *RI Lasix OR Salex tablets (40 mg).*
  1/2 tablet, oral, twice daily, until edema subsides.

+ *RI Potassium syrup 15% (10 mEq/5 ml).*
  One teaspoon (5 ml), oral, 3 times daily, until diuretic therapy is discontinued.

2. **2. A child, 5 years old (20 kg) with frequently relapsing nephrotic syndrome.**

RI Hostacortin OR Hostacortin H tablets (5 mg).
8 tablets, as a single oral dose, every other day (in the morning with breakfast) for 12 months.

+ *RI Cytoxan OR Endoxan tablets (50 mg).*
  One tablet, oral, daily for 8 weeks.
  (Discontinue if total leukocytic count is below 5000/cmm).

3. Urinary Tract Infection

Management of urinary tract infection in children includes the following:

1. Specific antibacterial therapy: Choice of the suitable antibacterial drug should ideally be based on the results of urine culture and sensitivity studies. However, in acute severe conditions, treatment should begin without waiting for results. In empirical drug therapy, the chosen drug, as well as the route of administration, depend primarily on the site of infection.

(a) In acute cystitis (dysuria, frequency, urgency or enuresis), the use of an oral antibacterial drug for 7 - 10 days is usually sufficient. The choices are:

- Co-trimoxazole: 20 mg/kg/day of sulphamethoxazole and 4 mg/kg/day of trimethoprim, given in 2 divided doses, every 12 hours.
- Ampicillin or amoxicillin: 50 mg/kg/day, in 3 divided doses, every 8 hours.
- First-generation Cephalosporins (as cephalexin, cephradine or cefadroxil) in a dose of 50 mg/kg/day, in 3 divided doses, every 8 hours.
- Second-generation cephalosporins (as cefaclor) in a dose of 50 mg/kg/day, in 3 divided doses, every 8 hours.
- Nitrofurantoin: 5 - 7 mg/kg/day, in 3 divided doses. It is a very effective drug and it has the advantage of being active against klebsiella and enterobacter.

* In Egypt, the drug is only available in tablet or capsule form:

RI Colifuran tablets (100 mg).
RIMacrofuran capsule(50 mg).

(b) In acute pyelonephritis (high fever, rigors and back pain), parenteral antibiotic therapy is preferable and duration of therapy should extend to 10-14 days. The following 2 drugs can be used together:

- Aminoglycoside as gentamicin (3 mg/kg/day), tobramycin (3 mg/kg/day) or amikacin (15 mg/kg/day). The drug is given I.M., divided into 2 equal doses.
- Second or third-generation cephalosporin as cefuroxime or cefotaxime. The dose is 50-100 mg/kg/day, I.M., divided into 2 equal doses.

2. Other measures and drugs: Excess fluid intake is important to wash the urinary system. Antipyretics as paracetamol (10 mg/kg/dose) or ibuprofen (10-15 mg/kg/dose) can be used for associated fever. Other drugs of particular relevance are:

(a) Bladder analgesics: These drugs can be used in older children with severe dysuria to relieve pain. Phenazopyridine is the mainly used drug. It is given orally in a dose of 10 mg/kg/day in 3 divided doses.

* Available preparations are:

RI Urisept tablets (100 mg).
RI Carmurit -T tablets (25 mg + 100 mg trimethoprim).

(b) Alkalinizing agents: Preparations containing sodium bicarbonate or sodium citrate may be used to change the urine pH. These agents are particularly useful when aminoglycosides are used. The average dosage is one teaspoon of effervescent granules, added to some water, to be taken orally twice daily.
* Available preparations are:

RI Magnesium effervescent salt.
RI Epimag OR Citromag OR Coliurinal effervescent granules.

3. Evaluation of therapy: Urine should be re-cultured 3 days after initiation of therapy to evaluate the response and it should be sterile. If the urine has not been sterilized, the antimicrobial agent should be discontinued and a new one is selected. Also, the urine should be re-cultured one week after the termination of therapy to ensure that the urine remains sterile. As urinary tract infections commonly recur, even without symptoms, urine culture every month, for at least 6 months, is advisable.

4. Management of recurrent infections: As a rule, each new infection is treated as a first infection (see above). If recurrences are frequent, a prophylactic long-term antibacterial treatment is indicated for 6 -12 months. The used drug is either **co-trimoxazole** or **nitrofurantoin**. The dose is only one-third the usual therapeutic dose and is given as a single daily dose. It is important to remember that broad spectrum antibiotics as amoxicillin or first- generation cephalosporins are usually ineffective for prophylaxis because of the rapid development of resistance.

- Frequently recurrent urinary tract infection necessitates certain investigation as:

1. Voiding urethrography to exclude vesicoureteral reflux. Prophylactic long-term antibacterial therapy is indicated in mild to moderate cases of vesico-ureteral reflux. In severe cases associated with structural changes in collecting system or with deteriorating renal function, surgical re-implantation of the ureter is indicated.
2. Intravenous pyelography to exclude obstructive uropathy.
3. Blood urea and serum creatinine level to evaluate the renal function.

Practical example

A child, 6 years old (20 kg) with acute cystitis.

RI Septrin OR Sutrim OR Chemotrim OR Septazole suspension.
One teaspoon (5 ml), oral, every 12 hours for 7 days.

OR RI Amoxil OR E-mox OR Moxipen suspension (250 mg/5 ml).
One and half teaspoon (7.5 ml), oral, every 8 hours for 7 days.

OR RI Ceporex OR Ospexin OR Keflex suspension (250 mg/5 ml).
One and half teaspoon (7.5 ml), oral, every 8 hours for 7 days.

OR RI Ceclor OR Bacticlor suspension (250 mg/5 ml).
One teaspoon (5 ml), oral, every 8 hours for 7 days.

4. Nocturnal Enuresis

Initial complete and unhurried **clinical assessment** is essential to determine the type and severity of the condition. Family history and history of emotional stresses are also important (see Pediatric Clinical Diagnosis).

Management of nocturnal enuresis includes the following aspects:

1. Treatment of organic causes: Urinary tract infection and polyuria should always be excluded especially in case of secondary enuresis. Many diabetic children present initially with the complaint of nocturnal enuresis. Full urine examination, urine culture and urinary output/24 hours are important initial steps.

2. Simple measures: These measures are indicated in children above the age of 4 years with primary enuresis:

- Fluid restriction after dinner.
- Let the child urinate before sleep.
- Wake the child up by night to urinate.
- Simple and immediate rewarding for dry-nights. Punishment, threats and humiliation should be totally avoided, as they may aggravate the condition. On the other hand, understanding and encouragement are commonly helpful.
- Bladder stretching exercises: Sometimes, trials to increase the intravesical pressure necessary to initiate micturition are useful. It is done by training the child during the day to drink much fluid and hold the urine as much as possible.
- Occasionally, the use of an electric buzzer ***(Beta for nocturnal enuresis)*** is helpful to wake up the child to urinate once the diaper gets wet.

3. Drug therapy: It is only indicated in children above the age of 6 years with primary nocturnal enuresis.

(a) Imipramine: The mechanism of action of this tricyclic antidepressant is probably through increased secretion of antidiuretic hormone. Treatment is started with 25 mg (one tablet) given as a single dose, one hour before bedtime. If the response is unsatisfactory within 2 weeks, the dose can be increased to 50 mg (two tablets). The dose can be also increased to 75 mg in children above 9 years. If no response after a trial of one month, the drug should be discontinued. In case of favorable response (60% of cases), the drug should be continued with the same dosage for another 2 months after which, gradual tapering of the dose is made over 4 - 6 weeks, before discontinuation. The most commonly accepted regimen for tapering is to give the dose once every other night for 3 weeks followed by once every third night for another 3 weeks. In case of relapse after the therapy has been stopped, it is important to wait for 1-2 months before restarting therapy. Available preparations are ***Tofranil tablets (25 mg).***

(b) Desmopressin (DDAVP): It is a synthetic vasopressin analogue chemically known as Desamine D Arginine Vasopressin. It is mainly used in treatment of diabetes insipidus due to antidiuretic hormone deficiency, but it was also found to be effective in nocturnal enuresis. Currently, it is considered as the drug of choice in management of nocturnal enuresis. The drug is given intranasal at bedtime in a dose of 10 mcg. If no response within 2 weeks, the dose can be increased to 20 mcg. In children above the age of 9 years, a dose as high as 40 mcg can be used. The main disadvantage of the drug is its price (very expensive drug). In case of favorable response, the drug is continued for several weeks followed by gradual withdrawal. Available preparations are ***(Minirin tablets, 0.1 mg)*** and ***(Minirin tablets, 0.2 mg).*** Treatment can be started with a dose of 0.1 mg, which can be increased to 0.2 mg or even 0.3 mg in case of unfavorable response.

(c) Other drugs: Spasmolytics as **oxybutynin** may be useful through increasing bladder capacity. Available preparations are ***Uripan OR Detronin syrup (5 mg/5 ml) and Uripan OR Detronin tablets (5 mg)***. The dose for school age children is one to two teaspoons or one to two tablets at bedtime.

4. Psychotherapy: It is not the first treatment of choice for enuresis, but it can be of value in secondary or coexisting emotional problems. It should be considered in older children when the child becomes ashamed, oversensitive or depressed because of the symptom. If psychotherapy is indicated, the patient and family should be referred to a qualified pediatric psychiatrist.

Practical examples

1. A child, 7 years old (22 kg) with primary nocturnal enuresis.

RI Tofranil OR Toframine tablets (25 mg).
One tablet at bedtime for 2 months (in case of favorable response), then one tablet every other night for 3 weeks followed by one tablet every third night for another 3 weeks.

RI Uripan OR Detronin syrup (5 mg/5 ml).
One teaspoon, oral, at bedtime.

+ ***Simple measures.***

2. A child, 8 years old (25 kg) with primary nocturnal enuresis and not responding to imipramine therapy.

RI Minirin tablets (0.2 mg).
One tablet, oral, at bedtime. If no response after 2 weeks, increase to 2 tablets or even 3 tablets in severe cases. In case of favorable response, continue for 6 weeks and then withdraw over another 6 weeks.

5. Acute Renal Failure

Patients with acute renal failure should be hospitalized, preferably in an intensive care unit. Prior to therapy, initial clinical and laboratory evaluation is essential to determine the type and the degree of renal insufficiency.

Clinical evaluation should include the level of consciousness, the state of hydration, blood pressure, cardiac condition and the urinary output.

Laboratory evaluation includes assessment of acid-base status (blood gases), serum electrolytes (Na, K, Ca, P) and renal function (blood urea and creatinine). ECG monitoring is important for detection of cardiac arrhythmias due to hyperkalemia.

Management includes conservative and dramatic measures.

A) Conservative measures

1. Treatment of oliguria or anuria: It is initially important to differentiate between prerenal failure (due to hypovolemia) and intrinsic renal failure (due to glomerular or tubular disease). Dehydration, blood loss or hypotension usually indicates prerenal origin. Treatment of oliguria is by the following steps:

(a) Correction of hypovolemia by volume expanders: It is indicated in case of dehydration, blood loss or hypotension. Isotonic saline or Ringer's lactate is given I.V., 20 ml/kg, over 30 minutes. Following this infusion, the dehydrated patient will usually void within 2 hours. Failure of urination after 2 hours indicates an intrinsic renal failure and the next step becomes indicated.

(b) Induction of diuresis by diuretics: It is indicated in oliguric patient who is not hypovolemic or who failed to respond to volume expanders. **Furosemide** is given I.V. in a dose of 2 mg/kg. If no response within one hour, a second dose of 10 mg/kg may be given. **Mannitol 20%** can be also used in a dose of 5 ml/kg, I.V. over 30 minutes. This diuretic therapy may succeed to convert the oliguric renal failure into non-oliguric renal failure, which is easier to manage especially for fluid overload and hyperkalemia. In absence of hypertension, **dopamine infusion** (5 mcg/kg/minute) may be added to increase renal cortical blood flow.

(c) Fluid restriction: It is indicated in patients who failed to obtain an adequate urine flow following volume expanders or diuretic therapy. The total daily fluid intake should equal the insensible water losses (which is about 300 ml/day) plus the urinary output of the previous day. In case of volume overload, a negative fluid balance is required where the total daily intake should be less than the calculated amount. The used intravenous solution should be made of glucose 5 or 10% and isotonic saline in a ratio of 4:1. Potassium should not be added to the solution until an adequate urine flow is obtained.

2. Treatment of acid-base and electrolyte disturbances: Metabolic acidosis, hyperkalemia, hyperphosphatemia, hypocalcemia and hyponataremia are the most commonly encountered problems.

(a) Treatment of metabolic acidosis: Moderate degree of metabolic acidosis is always present in acute renal failure. Severe acidosis with pH below 7.15 and bicarbonate below 10 mEq/liter requires an urgent therapy to raise pH above 7.2 and bicarbonate above 12 mEq/liter. **Sodium bicarbonate 5%** is given in a dose of 4 ml/kg over 10 minutes. Blood gas analysis is repeated after 30 minutes and the dose can be repeated if necessary. Other causative factors as anoxia or shock should be corrected, if present. (See I.V. fluid therapy).

(b) Treatment of hyperkalemia: Serum potassium level above 6 mEq /liter is serious and may lead to cardiac arrhythmia (tall peaked T wave and depressed S-T segment) and death. All foods, fluids or drugs should be free of potassium until an adequate urine flow is established. With potassium level near or above 7 mEq/liter, the following emergency measures are indicated:

- ***Calcium gluconate 10%:*** 0.5 ml/kg, I.V. over 10 minutes. Monitoring of the heart rate during infusion is essential. Calcium will counteract potassium effect on the myocardial irritability. Duration of action is only one hour.
- ***Sodium bicarbonate 5%:*** 4 ml/kg, I.V.over 10 minutes. Bicarbonate lowers potassium level through correction of acidosis and shift of extracellular potassium to intracellular compartment. Duration of action is about 2 hours.
- ***Glucose and insulin infusion:*** Glucose 50% (1 ml/kg) with regular insulin (1 unit for each 10 ml glucose 50%) is given I.V. over 1 hour. When glucose 50% is not available, glucose 25% can be used in a dose of 2 ml/kg with regular insulin, 1 unit for each 20 ml glucose 25%. Glucose and insulin infusion leads to shift of extracellular potassium to intracellular compartment. Duration of action is about 4 hours.
- ***Peritoneal dialysis:*** It is indicated in case of persistent hyperkalemia above 7 mEq/liter in spite of all above measures.

(c) Treatment of hyperphosphatemia and hypocalcemia: Hyperphosphatemia above 7 mg/dl necessitates therapy with aluminium hydroxide gel ***(Epicogel suspension).*** It is given orally or through a nasogastric tube in a dose of 2 ml/kg/day, divided into 4 doses. It lowers the serum phosphorus level through increasing fecal phosphate excretion. Lowering of serum phosphorus level usually corrects the hypocalcemia. Intravenous calcium gluconate 10% in a dose of 1 ml/kg over 10 minutes is only indicated in case of tetany.

(d) Treatment of hyponatremia: Fluid restriction is usually sufficient to correct the dilutional hyponatremia. With serum sodium level below 120 mEq/liter, cerebral edema may occur and therapy with **hypertonic saline 3%** is indicated. It is given I.V. in a dose of 5 - 10 ml/kg with the rate of 1 ml/minute. The dose can be repeated after 4 hours if serum sodium level is still below 120 mEq/liter. Each 1 ml/kg will raise the serum sodium level by about 1 mEq/liter.

3. Treatment of hypertension: Salt and water restriction is important. Severe hypertension is treated by I.V. diazoxide in a dose of 5 mg/kg given by rapid I.V. injection. Concomitant use of furosemide in a dose of 2 mg/kg should be considered. Mild to moderate hypertension can be treated with oral drugs.

4. Treatment of convulsions: Diazepam, given I.V. in a dose of 0.3 - 0.5 mg/kg is the drug of choice. Correction of the precipitating factors as hypocalcemia, hyponatremia or hypertension is equally important.

5. Treatment of anemia: Mild anemia is commonly present in acute renal failure. Small packed red cell transfusion (5 ml/kg) is only indicated when hemoglobin level falls below 7 gm/dl.

6. Control of infections: Unrecognized or uncontrolled infections account for one third of deaths in acute renal failure. Infections should be expected and properly diagnosed with appropriate cultures including blood and urine cultures. Two precautions regarding the choice of antibiotics and the drug dosage are important. Nephrotoxic drugs as aminoglycosides are better to be avoided. **Chloramphenicol** and **cefoperazone** ***(Cefobid)*** have the advantage of being mainly excreted through the liver. With marked renal insufficiency, dosage adjustment is made by reduction of dosage or frequency of administration.

7. Nutritional support: Nasogastric tube feeding or oral feeding should replace the I.V. fluids as soon as the clinical condition permits. If I.V. fluid therapy should be used for more than 4 days, aminoacid infusion ***(Vamin or Totamine)*** should be added in a dose of 10 ml/kg/day, given over 4 - 6 hours. Diet should be limited initially to carbohydrates and fats. Proteins can be allowed in small amounts during the recovery phase.

B) Dramatic Measures

1. Peritoneal dialysis: This dramatic measure is frequently life saving in infants and children with severe acute renal failure. The indications for peritoneal dialysis in acute renal failure are either clinical or laboratory:

(a) Clinical indications

- Deteriorating neurological state in spite of the conservative measures.
- Volume overload with congestive heart failure or pulmonary oedema.
- Gastrointestinal bleeding secondary to uremic platelet dysfunction.

(b) Laboratory indications

- Blood urea above 150 mg/dl.
- Persistent severe acidosis (pH below 7.1) especially with volume overload.
- Persistent hyperkalemia above 7 mEq/liter in spite of conservative measures.
- Hypernatremia above 160 mg Eq/liter or hyponatremia below 110 mEq/liter especially with volume overload.
- Hypercalcemia above 12 mg/dl.

Peritoneal dialysis depends on the idea that the peritoneum is a semipermeable membrane across which water and solute diffuse along their concentration gradient. Peritoneal dialysis is made by repeated cycles or runs of infusion and draining out of the dialysate solution. Initial cycles are made with 20 ml/kg/cycle and the amount is then increased gradually to a final range of 40-50 ml/kg/cycle. The dialysate solution should be warmed to 38°C before infusion, and the dialysis catheter can be left in place for up to 12 hours. Peritoneal dialysis should be only made with a personnel experienced with the technique and oriented with the suitable dialysate solutions and the possible complications.

2. Acute hemodialysis: It is a more efficient measure than peritoneal dialysis but it is also more difficult, more expensive and necessitates sophisticated expensive hemodialyzer, disposable filters and tubing. It is mainly indicated in situations where peritoneal dialysis is contraindicated as with infected abdominal wall, recent abdominal surgery, peritoneal adhesions or diaphragmatic defect. It depends on the same idea of peritoneal dialysis where water and solute diffuse across a semi-permeable membrane from blood to dialysate or vice versa along their concentration gradients. Acute hemodialysis can be made with either 2 catheters (venous and arterial), or one double-lumen catheter placed in a vein. Infants and children can safely tolerate a blood flow rate in the range of 2-5 ml/kg/minute. Mannitol 20% may be needed in a dose of 5-10 ml/kg, I.V. over 30 minutes in patients with blood urea above 150 mg/dl.

3. Hemofiltration: It is a form of continuous renal replacement therapy, which does not adversely affect the cardiopulmonary function as in peritoneal dialysis and hemodialysis. It can be used in the same indications but it is particularly useful in those with compromised cardiopulmonary function or with severe coagulopathies. It is a simple safe procedure with almost no contraindications. It can be made by one of two methods, continuous arterio-venous hemofiltration (CAVH) or continuous venovenous hemofiltration (CVVH). It depends on the idea that water and solutes are extracted from the blood by the development of a hydrostatic pressure gradient and subsequent filtration.

C) Treatment of the cause

Conservative and/or dramatic measures should be combined with the appropriate treatment of the causative disease. In prerenal causes, hypoxemia and shock should be urgently corrected with the nonspecific respiratory or cardiovascular support in addition to the specific treatment of the causative disease. In postrenal causes, urological consultation for relief of obstruction should be considered after the initial stabilization.

6. Chronic Renal Failure

Management of chronic renal failure requires proper understanding of the complex pathophysiological changes that occur. Periodic clinical and laboratory evaluation is essential to determine the degree or severity of renal insufficiency. Clinical evaluation should include nutritional status and growth, blood pressure, cardiac function and skeletal examination for rachitic changes.

Laboratory evaluation includes measurements of blood urea and creatinine, acid-base status, serum electrolytes (Na, K, Ca, P), hemoglobin level and radiological examination of bones for evidence of rachitic changes.

Measurement of glomerular filtration rate is important to determine the degree of renal insufficiency. Normal value is about 70 ml/minute/ m^2. With values between 20 - 30 ml/minute/m^2, manifestations of chronic renal failure appear, while values below 10 ml/minute/m^2 denote severe renal insufficiency. A simple method for calculating glomerular filtration rate (GFR) depends on the length and the serum creatinine level where:

$$\text{GFR} = \frac{0.5\ (\text{length})}{\text{serum creatinine}}$$

E.g., if the length is 120 cm and serum creatinine is 4 mg/dl, so:

$$\text{GFR} = \frac{0.5(120)}{4} = 15\ \text{ml/minute/m}^2$$

Management of chronic renal failure includes the following aspects:

A) Conservative measures

These measures are indicated in mild to moderate cases of renal insufficiency with GFR above 10 ml/minute/m^2. The goal of conservative measures is to preserve every functioning nephron as long as possible and to prevent complications. The main lines of therapy are:

1. Diet and water intake: Diet should be high in carbohydrates and fats (to provide sufficient calories) and low in proteins (to decrease the nitrogenous waste products). Proteins should be of high biological value as eggs, milk, meat and fish. The water intake is usually regulated by the thirst mechanism. Water and salt restriction are only indicated in presence of hypertension, oedema or congestive heart failure.

2. Treatment of chronic metabolic acidosis: With bicarbonate level below 18 mEq/liter, therapy with oral sodium bicarbonate is indicated. Sodium bicarbonate 5% is given orally in a dose of 2- 3 ml/kg/day in 2 divided doses.

3. Treatment of hyperphosphatemia and hypocalcemia: Serum phosphorus level should be kept below 6 mg/dl. This can be achieved by oral **aluminium hydroxide gel** ***(Epicogel or Mucogel suspension)*** given in a dose of 5 - 15 ml with each meal. If the serum calcium level remains low after correction of the serum phosphorus, oral **calcium** supplementation is added ***(Calcium Sandoz syrup, 110 mg elemental calcium/5 ml).*** It is given in a dose of 40 - 60 mg elemental calcium/kg/day, divided into 2 - 3 doses (Practical dosage is one teaspoon for each 2 - 3 kg/day). **Vitamin D** therapy is indicated in patients with persistent hypocalcemia in spite of the oral aluminium hydroxide gel and calcium therapy and also in those with radiological evidence of rickets. Vitamin D is given orally in a dose of 20.000 I.U./day ***(D-ca B_{12} amp., 20.000 unit/ampoule).*** The dose can be increased until serum calcium is normal and radiological healing of rickets appears. One alpha hydroxycholecalciferol, which is an expensive active form of vitamin D, can be used in resistant cases ***(One alpha drops, 0.1 mcg/drop).*** It is given orally in a dose of 0.05 mcg/kg/day (Practical dosage is one drop for each 2 kg/day).

4.Treatment of chronic hypertension: In addition to salt restriction and oral furosemide therapy (1-2 mg/kg/day), oral antihypertensive therapy is indicated. Propranolol (1 -4 mg/kg/day) and hydralazine (1 -4 mg/kg/day) can be used initially. Captopril (0.5 -2.0 mg/kg/day) is reserved for resistant cases.

5. Treatment of chronic anemia: Small packed red cell transfusion (5 - 10 ml/kg) is only indicated when hemoglobin level falls below 6 gm/dl. Iron supplementation is reserved for documented cases of iron deficiency.

6. Water soluble vitamin supplementation: Children with chronic renal failure commonly become deficient in water soluble vitamins (B and C) and regular supplementation of these vitamins is indicated. One or two teaspoons per day of any of the available preparations is sufficient (See vitamin therapy). Fat-soluble vitamin supplementation (A and K) is not required.

7. Control of infections: Severe urinary tract infection or any severe systemic infection may precipitate an episode of acute renal failure. Unfortunately, many patients with chronic renal failure are firstly diagnosed with acute renal failure. Infections should be promptly diagnosed and controlled with the appropriate antibiotic therapy (see acute renal failure).

B) Chronic dialysis

Chronic dialysis is indicated in patients with severe renal insufficiency (GFR below 10 ml/minute/m^2) and when conservative measures are no longer effective. Growth arrest, inability to carry out normal activities, persistent circulatory overload and severe renal osteodystrophy are clear indications. Chronic dialysis can be made by one of 2 methods:

1. Continuous ambulatory peritoneal dialysis (CAPO): Recently, it becomes the optimal form of chronic dialysis in children and largely replaced hemodialysis. Although it is not as efficient as hemodialysis, it has the advantages of simplicity, greater mobility, steady state of chemistries and better growth rate. The main disadvantage is the potential risk of infection.

2. Hemodialysis: It is only carried out in renal specialized centers using expensive equipment (hemodialyzer). Creation of an arteriovenous fistula is essential. It is made for 12 - 18 hours per week in one or 2 settings. Among the several disadvantages are growth retardation and psychological problems.

C) Renal transplantation

It is the ideal dramatic therapy for children with severe renal insufficiency (end stage renal failure). It can be carried out in children above the age of 5 years. Problems regarding the availability of histocompatible donor and immunological problems of graft rejection largely limit its widespread application.

Hemodialyzer



9

Hematology

1. Iron Deficiency Anemia.
2. G6PD Deficiency.
3. Cooley's Anemia.
4. Sickle Cell Anemia.
5. Other Hemolytic Anemias.
6. Idiopathic Thrombocytopenic Purpura (ITP).
7. Aplastic Pancytopenia.
8. Hemophilia.
9. Dissemintated Intravascular Coagulation (DIC).

1. Iron Deficiency Anemia

Iron deficiency anemia is by far the commonest hematological disorder in pediatric age group. It should be suspected in every case of prolonged breast-feeding, chronic diarrhea or repeated blood loss. Diagnosis should be confirmed by the presence of hypochromic microcytic anemia and low serum iron level.

Treatment of iron deficiency anemia includes the following aspects:

1. Iron therapy: Treatment with **oral** iron preparations is usually effective in most cases. The dose is 6 mg elemental iron/kg/day, divided into 2 -3 doses, between meals. Treatment should be continued for 2 -3 months to correct the anemia and to ensure repletion of iron stores. The response to iron therapy is rapid as appetite improves after 24 hours of initiation of therapy. From the fourth day, a steady rise of hemoglobin level occurs, and may be up to 0.5 gm/day. Failure of response to iron therapy should suggest poor absorption, continued blood loss, associated infection or wrong diagnosis. In case of chronic malabsorption, **intramuscular** iron dextran injection may be used ***(Iron Dextran amp., 250 mg/ 5 ml).*** The dose is 4 mg elemental iron/kg/dose, deep I.M., every other day for 3 -4 injections. Each dose will raise hemoglobin level by 1 gm/dl. (For treatment of accidental toxicity, see mineral therapy). **I.V iron** is recently available and can be used in severe cases ***(Ferosac I.V amp.,100 mg/5 ml).***

2. Packed red cell transfusion: It is only indicated in severe cases with hemoglobin level below 5 gm/dl. The given amount per time should not exceed 5 ml/kg to avoid aggravation of the already present state of hypervolemia. Observation of the heart rate during infusion is important. Single or twice transfusions are usually sufficient to raise hemoglobin to safe levels.

3. Treatment of the cause: In nutritional cases, correction of the dietetic error is as important as iron therapy. As both breast milk and fresh cow's milk are deficient in iron, introduction of foods rich in iron as egg yolk, meat and liver is important. Chronic diarrhea should be treated and ankylostoma infestation should be considered as a cause of repeated blood loss in endemic areas.

Practical example

A child, 2 years old (10 kg) with iron deficiency anemia.

RI Ferromix syrup (15 mg elemental iron/5 ml).
2 teaspoons (10 ml), twice daily, between meals for 8 weeks.

OR RI Sytron syrup (27 mg elemental iron/5 ml).
One teaspoon (5 ml), twice daily, between meals for 8 weeks.

OR RI Vitaferrol OR Rubraton-B Elixir (38 mg elemental iron/5 ml).
3/4 teaspoon (4 ml), oral, twice daily, between meals for 8 weeks.

2. G6PD Deficiency

Glucose 6-phosphate dehydrogenase deficiency (G6PD) is a common cause of acute hemolysis in mediterranean areas. In Egypt, the condition is usually discovered accidentally in late infancy as an acute hemolytic episode following ingestion of broad beans. As the condition is an x-linked disease, only males are affected. Confirmation of the clinical diagnosis by study of the enzymatic activity of G6PD should not be made except after 3 weeks of the hemolytic episode (see Pediatric Clinical Diagnosis).

Management of G6PD deficiency includes the following aspects:

1. Treatment of the acute hemolytic crisis: In mild hemolytic episodes, the condition may pass unnoticed, but in moderately severe crises, characterized by intense pallor and red urine, urgent packed red cell transfusion (10 ml/kg) is life saving. Oxygen therapy until the blood is available, and during transfusion is important to correct the acute hypoxia. The acute hemolytic episode will subside spontaneously within 24 - 36 hours.

2. Prevention of subsequent hemolytic crises: Once the diagnosis is established, avoidance of exposure to oxidant materials is the most important aspect of management. A list containing the oxidant materials (foods and drugs) should be offered to the parents. The list includes:

(a) Foods to be avoided: Broad beans and its products are the most potent oxidant materials. Fava bean also should be avoided. Other beans as green beans and peas may induce hemolysis in some patients. Avoidance of these foods may be lifelong.

(b) Drugs to be avoided: Antipyretics as acetylsalicylic acid (aspirin) or metamizole (novalgin) should be avoided. Paracetamol is safe. Some antibiotics as chloramphenicol, nalidixic acid and furazolidone are potent oxidants. Sulphonamides also should be avoided. It is important to remember that several antidiarrheal preparations contain sulphonamides. Antimalarials also can induce hemolysis.

3. Genetic counseling: Parents should know that the condition is an x-linked disease, transmitted by the asymptomatic mother to affect 50% of her sons. So, the recurrence rate in subsequent pregnancies is 50% in male offsprings. In male siblings (brothers) of a patient, the enzymatic activity of G6PD should be studied for early diagnosis.

3. Cooley's Anemia

Beta thalassemia major is the commonest cause of chronic hemolytic anemia in Egypt. Unfortunately, there is no specific curative therapy and the treatment is mainly supportive and aims to keep hemoglobin level between 10 - 12 gm/dl to prevent or minimize the effects of hemosiderosis. With current therapy, only few patients survive into adult life.

Management of cooley's anemia includes the following aspects:

1. Hypertransfusion therapy: Repeated packed red cell transfusions (15-20 ml/kg), every 4 - 6 weeks is important to keep the hemoglobin level between 10 -12 gm. Maintenance of the hemoglobin at this level is associated with better clinical response (good activity and well-being) and lesser incidence of complications (marrow hyperplasia, progressive splenomegaly, facial bony changes and cardiac dilatation). Certainly, patients with hemoglobin level above 10 gm have a better life expectancy than those with lower values.

2. Drug therapy: As hemosiderosis and cardiac siderosis are the causes of death, removal of excess iron by iron-chelating agents is important and may have the potential for prolonging life expectancy. **Deferoxamine** ***(Desferal vial, 500 mg)*** is the mainly used chelating agent. It is given intramuscular as a single daily injection in a dose of 20-40 mg/kg/day, 5 days a week. Recently, deferoxamine subcutaneous administration over 8 - 12 hours during sleep, 5 days per week is found to be more effective. A special battery-operated infusion pump is required for the subcutaneous administration. In a significant number of patients, relative folic acid deficiency is present, so routine daily administration of **folic acid** ***(Folic acid tablets, 5 mg)*** in a dose of 5 mg (one tablet) is recommended.

3. Splenectomy: It is indicated when transfusion requirements become progressively greater and also in those with massive splenomegaly causing abdominal discomfort and distension. The operation should not be made before the age of 5 - 6 years to minimize the risk of post-splenectomy overwhelming infections. Prophylactic oral penicillin therapy with phenoxymethyl penicillin ***(Ospen suspension, 400.000 unit/5 ml)*** for one year following the operation is recommended. Infections should be treated vigorously.

4. Bone marrow transplantation: It can be done for patients who have non-affected histocompatible siblings. Although it is a curative therapy, the procedure is risky with considerable morbidity and mortality.

5. Genetic counseling: Parents should realize that the recurrence rate in subsequent pregnancies is 25%.

4. Sickle Cell Anemia

Sickle cell anemia is primarily found in black Africans. It is occasionally seen in North Africa and in the Middle East. As most other inherited chronic hemolytic anemias, there is no known effective therapy that can reduce the rate of chronic hemolysis or prevent crises. Many patients die in early adult life with progressive renal or heart failure.

Management of sickle cell anemia includes the following:

1. Treatment of acute crises: Several acute episodes may occur in patients with sickle cell anemia:

(a) Vaso-occlusive (painful) crises: It is the most common type, which may occur spontaneously or in response to infections. It is characterized by painful swellings of the hands and feet (hand-foot syndrome) and painful swellings of large joints. The condition may be associated with severe abdominal pain and picture resembling pneumonia. Treatment is by:

- Analgesics: Ibuprofen or diclofenac can be used oral or rectal, in divided doses (see antipyretics).
- Sedatives: Diazepam or midazolam can be used oral or parentral in divided doses (see sedatives and hypnotics).
- Hydration and correction of acidosis by I.V. fluids are important.
- Oxygen therapy is also important especially with pulmonary symptoms.
- Prolonged severe painful crises can be terminated by whole blood or packed red cell transfusion. Partial exchange transfusion, if possible, is rapidly effective.
- Control of infection, if it is the precipitating factor.

(b) Sequestration crises: Where large amount of blood become acutely pooled in the liver and spleen. Treatment is by hydration and whole blood transfusion.

(c) Aplastic and hyperhemolytic crises: Packed red cell transfusion (10 - 15 ml/kg) and control of precipitating infections.

2. Treatment of infections: Patients with sickle cell anemia are particularly susceptible to pneumococcal meningitis and septicemia and to salmonella osteomyelitis. As these infections may be the cause of death, early vigorous control is important.

3. Splenectomy: It is only indicated in hypersplenism or in frequently recurrent sequestration crises.

4. Genetic counseling: Parents should know that the recurrence rate in subsequent pregnancies is 25%.

5. Other Hemolytic Anemias

1. Hereditary spherocytosis

It is the most common form of chronic hemolytic anemia in North Europe. It is transmitted as autosomal dominant trait but 25% represent new mutations. **Splenectomy** is the main line of therapy as it produces clinical cure. After the operation, jaundice and reticulocytosis disappear and the hemoglobin level attains the normal range, despite the persistent spherocytosis. The operation should not be performed before the age of 5 - 6 years. Prophylactic oral penicillin for one year following the operation is recommended.

2. Pyruvate kinase deficiency

It is the commonest form of chronic hemolytic anemia due to enzymatic deficiency. Clinical manifestations vary from a mild unnoticed disease to a severe anemia requiring repeated transfusions. **Splenectomy** is not curative, but it is indicated in severe cases requiring frequent transfusions. Again, the operation should not be performed before the age of 5 - 6 years.

3. Autoimmune hemolytic anemia

It is the commonest form of acquired hemolytic anemia. In the acute form, prognosis is good and full recovery within 3 months is the rule. In the chronic form, the response to therapy is variable and mortality rate may approximate 10%. Strongly positive direct Coombs test is the constant diagnostic laboratory finding in both forms. If the condition is associated with immune thrombocytopenia (Evans syndrome), the prognosis becomes bad. Treatment includes the following aspects:

1. Packed red cell transfusion: 10-15 ml/kg of packed red cells are required to correct the severe anemia. Careful cross matching is important. At times, it may be difficult to find a compatible blood.

2. Corticosteroids: Prednisone is given orally in a dose of 2-4 mg/kg/day in divided doses. Treatment is continued until the hemolytic process is controlled, then the dose is gradually reduced. If relapse occurs, a full dosage therapy should be resumed.

3. Splenectomy: It is only indicated in chronic cases not responding to corticosteroid therapy.

4. In chronic cases secondary to systemic lupus or lymphoma, treatment of the primary disease is the main therapy.

6. Idiopathic Thrombocytopenic Purpura (ITP)

It is the most common form of thrombocytopenic purpura in childhood. Diagnosis depends on the presence of severe thrombocytopenia (platelet count below 20.000/mm^3) and on clinical and laboratory exclusion of other causes of acute and chronic purpura (see pediatric clinical diagnosis).

Management of ITP includes the following aspects:

1. Corticosteroid therapy: It is almost indicated in all cases to ensure rapid recovery and to prevent serious hemorrhage. In cases not associated with significant hemorrhage, prednisone is given orally in a dose of 1 - 2 mg/kg/day in divided doses. In case of severe hemorrhage or when intracranial hemorrhage is suspected, the dose should be increased to 5-10 mg/kg/day. Corticosteroid therapy is continued until platelet count is normal or for 3 weeks, which ever comes first. 75% of cases recover completely within 3 weeks and most of others within 8 weeks. If thrombocytopenia persists for 4 -6 months, a second course of prednisone for 3 weeks is indicated.

2. Fresh blood or platelet transfusions: Fresh blood transfusion (20 ml/kg) is indicated to compensate for blood loss in case of significant hemorrhage. Platelet transfusion may be considered to cause temporary rise in platelet count especially when serious hemorrhage, as intracranial hemorrhage, is suspected.

3. Intravenous immunoglobulins (IVIG): I.V infusion of IG is very useful to induce rapid rise in platelet count within 48 hours in 95% of cases. IVIG is given in a dose of 300 mg/kg/day, I.V., over 6-8 hours, for 4-5 days. The available preparations are ***Sandoglobulin, I.V globulin or Vigam.*** Practical dosage is 10 ml/kg (Sandoglobulin, 30 mg/ml) or 6 ml/kg (I.V globulin or Vigam, 50 mg/ml) .... I.V infusion over 6-8 hours daily, for 4-5 days (For details, see passive immunization). It is important to remember that therapy with IVIG is both very expensive and time consuming.

4. Splenectomy: It is only indicated in chronic cases with persistent thrombocytopenia for more than one year. Most cases will improve after the operation. Fortunately, only 2% of cases tend to be chronic and resistant to corticosteroids and splenectomy. In these cases, immunosuppressive drugs as vincristine may be tried.

7. Aplastic Pancytopenia

The prognosis of aplastic pancytopenia is generally poor. In the congenital form (Fanconi anemia), survival for many years can be achieved with androgen and corticosteroid therapy, but ultimately death from infections or uncontrolled hemorrhage will occur. In the acquired form, the prognosis is worse as the response to therapy is poor and 70% of cases will die within 6 months of onset. Even in the lucky 10-20% of cases who recover, acute leukemia may develop.

Management of aplastic pancytopenia includes the following aspects:

1. Drug therapy: A combination of androgens and corticosteroids is initially used to stimulate the aplastic bone marrow. **Testosterone** ***(Proviron tablets, 25mg),*** is given orally in a dose of 2-4 mg/kg/day. **Corticosteroids** as prednisone ***(Hostacortin tablets, 5 mg)*** or methylprednisolone ***(Urbason tablets, 4 mg and 8 mg)*** is also used in a small dosage (1 mg/kg/day, orally) to enhance the effect of androgens and to reduce the tendency to bleeding. The hematological response to therapy, if it happens, becomes evident after 2-4 months of onset. Recently, **Cyclosporine,** which is a potent immunosuppressant agent, can be added in resistant cases in a dose of 5-10 mg/kg/day, orally. The drug is available in syrup and capsule forms ***(Abrammune or Sandimmun syrup, 100 mg/ml and Abrammune or Sandimmun capsules, 50 mg and 100 mg).*** As the drug is nephrotoxic, monitoring of renal function during its use is essential. If remission occurs, gradual withdrawal of therapy is made. In Fanconi anemia, continuous therapy is almost required.

2. Replacement therapy: Repeated whole blood transfusion and platelet transfusion are usually required to compensate for blood loss and to raise the level of red cells, white cells and platelets. Whole blood is transfused in an amount of 20 ml/kg, during bleeding episodes.

3. Prevention and control of infections: Serious and life-threatening infections due to neutropenia are a common cause of death. Severely ill children should be protected from infections by being placed in **"reverse isolation".** Infections should be promptly recognized and vigorously treated by appropriate antibiotics and according to culture and sensitivity studies.

4. Bone marrow transplantation: In refractory cases and when a histocompatible sibling is available, bone marrow transplantation is indicated and a up to 90% success rate can be achieved.

5. New lines of therapy: Antithymocyte globulin (ATG), either alone or in combination with corticosteroids, cyclosporine and bone morrow transplantation is currently considered as the treatment of choice.

8. Hemophilia

Hemophilia A or classic hemophilia accounts for about 80% of cases of hemophilia. It is an X-linked disease carried by asymptomatic females to affect their sons. The activity of factor VIII is markedly reduced to 0 -5% of normal in moderate to severe cases. Management of the hemophilic child includes the following aspects:

A) Treatment of bleeding episodes

When bleeding occurs, several urgent measures are necessary to control bleeding. These measures include replacement therapy, drug therapy and local hemostatic measures.

1. Replacement therapy: The aim of this therapy is to compensate for blood loss and to raise factor VIII level in the blood to hemostatic level (above 20%). This can be only achieved by I.V. infusion of one or more of the followings:

(a) Fresh whole blood: Infusion of 20 ml/kg of freshly drawn blood is useful to compensate for blood loss, but it will not raise factor VIII activity to a hemostatic level, so other measures are usually required.

(b) Fresh frozen plasma: 10 - 15 ml/kg are immediately infused (each 1 ml of plasma contains 1 unit of factor VIII). As the in vivo half-life of factor VIII is only 12 hours, the same amount (10 -15 ml/kg) should be given every 12 hours until bleeding stops. Infusion should be as rapid as the patient can tolerate to achieve peak levels. 10 ml/kg of fresh frozen plasma will raise the activity of factor VIII to 20%.

(c) Factor VIII concentrates: Several preparations containing factor VIII are available and can be used to achieve high levels of factor VIII. They are mainly useful in severe, life-threatening hemorrhage or before surgery. **Antihemophilic plasma** ***(Cryoprecipitate bags, 125 units/25 ml)*** is the least expensive. Each bag is prepared from 250 ml plasma. It is given I.V. in a dose of 5 ml/kg (25 units/kg) every 12 hours until bleeding stops. 5 ml/kg of antihemophilic plasma will raise factor VIII activity to about 50%. **Pure factor VIII concentrates** are also available in a lyophilized powder form that can be reconstituted just before use ***(Kryobulin, 250 or 500 units/20 ml).*** A single infusion of 25 units/kg is usually sufficient to control bleeding, as it will raise factor VIII level to about 50%. In case of life-threatening hemorrhage, as intracranial hemorrhage, continuous infusion of factor VIII in a dose of 2 units/kg/hour is used to maintain steady level of factor VIII above 50%. In case of major surgeries, the continuous infusion is maintained for up to 2 weeks.

2. Drug therapy: Recent studies indicate that the administration of **desmopressin**, either nasal ***(Minirin nasal spray, 10 mcg/puff)*** or oral ***(Minirin tablets, 0.1 mg)*** is useful to raise factor VIII level and can be used in mild to moderate bleeding episodes. It is given intranasal in a dose of 10 mcg/day or orally in a dose of 0.1-0.2 mg/day until bleeding stops. The drug is usually not useful in severe episodes. Desmopressin is a synthetic analogue of antidiuretic hormone and is mainly used in diabetes insipidus and nocturnal enuresis (see hormonal therapy and nocturnal enuresis).

3. Local hemostatic measures: Application of cold and pressure on bleeding sites is as important as factor VIII therapy. Epistaxis usually needs pressure over the bleeding site for 10 minutes followed by insertion of a pledged wet with a vasoconstrictor nose drops or adrenaline. At times, the insertion of a small piece of gelatin sponge ***(Gelfoam)*** may be effective. In hemarthrosis, immobilization for 2 days followed by gradual passive exercise is usually sufficient. In a severely painful joint with very tense overlying skin, aspiration of blood, after adequate factor VIII therapy, will provide some relief.

B) Protective measures

In between episodes, some measures are important to prevent bleeding and to avoid complications of repeated transfusions.

1. Prevention of trauma: The hemophilic infant or child should be carefully observed. In infancy, the crib or bed should be padded and close observation while learning crawling and walking is important. In childhood, activities and sports that carry the risk of trauma should be avoided. On the other hand, overprotection with its psychological adverse effects should be avoided.

2. Avoidance of aspirin: Aspirin may provoke severe hemorrhage in hemophilic patients through its effect on platelet functions.

3. Immunization against hepatitis B: As a consequence to repeated transfusions, the risk of hepatitis B infection is great. Vaccination against hepatitis B, given in early infancy, is recommended. The vaccine is given I.M. in 3 doses (see immunization)

C) Genetic counseling

Parents should realize that the disease is an X-linked disease, carried by the asymptomatic mother to affect 50% of her sons. The recurrence rate in subsequent pregnancies is 50% in male offsprings. Also 50% of her daughters will be carriers as their mother.

Notice

In hemophilia B and hemophilia C, fresh frozen plasma (10-15 ml/kg) every 12-24 hours is the main line of therapy. Factor VIII concentrates are of no value. Factor IX concentrates are present but not yet available in Egypt.

9. Disseminated Intravascular Coagulation (DIC)

DIC usually occurs as a complication of another critical illness. Sick neonates with hypoxia, acidosis and septicemia and infants with gastroenteritis and dehydration are the commonest causes. Clinical manifestations are usually over-shadowed by the primary disease (For clinical and laboratory diagnosis, see Pediatric Clinical Diagnosis).

Management of DIC includes the following aspects:

1. Prompt control of primary illness: Early recognition and treatment of the precipitating factors is the most important line of therapy. Hypoxia, Shock, acidosis and gram-negative septicemia are the main predisposing factors. Bleeding and abnormal laboratory findings quickly improve, if these factors are adequately controlled.

2. Replacement therapy: Correction of the hematological defects may be necessary in severe cases.

(a) Platelet concentrates: It is indicated in severe thrombocytopenia. It is given in an amount of 2 ml/kg, I.V. every 12 hours. Although platelet count may not rise dramatically, manifestations of bleeding usually lessen.

(b) Fresh frozen plasma: 10 ml/kg, I.V. every 12-24 hours may be required to replace fibrinogen, prothrombin and other deficient factors.

(c) Fresh whole blood or packed red cells: 10 ml/kg may be needed to correct anemia and to compensate for blood loss.

(d) Exchange transfusion: In neonates who cannot tolerate the volume load or when life-threatening hemorrhage occurs, exchange transfusion is an appropriate therapy.

(e) Vitamin K1: 5 mg of vitamin K1 should always be given I.V. especially when the patient is on I.V. fluids for several days.

3. Heparin therapy: Most patients with DIC can be managed without heparinization. It is only indicated when widespread cutaneous thrombosis is evident as in purpura fulminans. If used, the dose is 50 - 100 units/kg every 4 hours, I.V. ***(Heparin amp, 5000 units/ml).*** Practical dosage is 0.2 ml/kg of the diluted solution (1 ml + 9 ml saline).

10

Endocrinology

1. Hypothyroidism.
2. Type I Diabetes Mellitus.

1. Hypothyroidism

Early diagnosis of congenital hypothyroidism is important if physical and mental developments are to be preserved.

Recently, **neonatal thyroid screening program** is available for all newborns in Egypt from the third to seventh day after birth. A blood drop is obtained by heel prick on a filter paper and is analyzed for TSH and T_4. If TSH value is above 20 µU/L, an immediate blood sample is withdrawn and reanalyzed for TSH and T_4. Diagnosis depends on the presence of elevated TSH level above 20 mU/L with low T_4 below 5 mcg/dl.

With clinical suspicion in neonatal period or infancy, measurement of T_4, T_3 and TSH levels is essential .

Treatment of congenital hypothyroidism depends on **life long therapy with thyroxine.** The drug is given orally in a dose of 8 - 10 mcg/kg/day, as a single daily dose ***(Eltroxin tablets, 50 mcg and 100 mcg).***

Evaluation of response: Initial response to therapy dose not appear before 2 weeks of onset and maximum response usually occurs after 6 weeks. Signs of therapeutic response are: increased activity and alertness, improvement of skin colour and temperature and reversal of all symptoms and signs. On the other hand, signs of overdosage include irritability, restlessness, diarrhea and abdominal cramps. Serum level of T_4 and TSH should be checked, 4 - 6 weeks after initiation of therapy. Dosage is adjusted to keep serum level of T_4 in the range of upper half of normal level. As treatment is life long, dosage is adjusted according to the body weight. During childhood, dosage is only 4 -6 mcg/kg/day.

Practical example

An infant, two months old (5 kg) with congenital hypothyroidism.

RI Eltroxin tablets (50 mcg).

One tablet (crushed), oral, once daily.

- Evaluate the clinical response after 2 weeks, 4 weeks and 6 weeks.
- Repeat T_4 and TSH after 6 weeks.
- Adjust the dosage according to body weight and the response.
- In childhood, dosage is only 4 - 6 mcg/kg/day.

  e.g. : At 6 years (20 kg), give:

  RI Eltroxin tablets (100 mcg).

  One tablet, once daily.

Notice

- Normal level of T_4 is 5-12 mcg/dl.
- Normal level of TSH is below 5 mU/L

2. Type I Diabetes Mellitus

Management of type I diabetes can be classified into 3 phases:

1. Diabetic ketoacidosis: During this phase, management aims at:

- Correction of shock, acidosis and dehydration by I.V. fluid therapy.
- Correction of hyperglycemia and CHO metabolism by insulin therapy.
- Control of infection, when it is the precipitating factor.

This phase usually takes 36 - 48 hours. The insulin used during this phase is the regular insulin and it is given by I.V. continuous infusion.

2. Post-acidotic phase or phase of initial adjustment: During this phase, management aims at:

- Initiation of oral feeding.
- Calculation of insulin dosage required for keeping blood sugar between 100 - 180 mg/dl.
- Careful observation to avoid insulin shock on one side or return to hyperglycemia on the other side.

This phase usually takes 2 - 3 days. The insulin used during this phase is the regular insulin and it is given subcutaneous every 6 - 8 hours before meals.

3. Life-long management: During this phase, management aims at:

- Keeping fasting blood sugar between 80 - 120 mg/dl and post-prandial level between 100 - 150 mg/dl.
- Prevention of ketoacidosis or hypoglycemia.
- Achievement of normal growth and normal activity.

Treatment during this phase is life long. The insulin used in therapy is a combination of intermediate insulin and regular insulin, given as three or two daily subcutaneous injections.

*** It is important to remember that:**

- In patients presenting with the picture of diabetic ketoacidosis, management will include the 3 phases of management.
- In patients presenting with polyuria and polydipsia, but without ketoacidosis, management will start from the second phase (phase of initial adjustment).
- Hospitalization during the first 2 phases is essential.

A) Management of diabetic ketoacidosis

Diabetic ketoacidosis is a medical emergency requiring constant attention and teamwork among physician, nurse and laboratory.

When it is not known that the patient is diabetic, the clinical triad of

Metabolic acidosis (deep rapid respiration), dehydration and coma in a child should always raise the possibility. Diagnosis is confirmed by the following:

1. Hyperglycemia above 300 mg/dl.
2. Metabolic acidosis (pH below 7.3 and bicarbonate below 15 mEq/liter).
3. Glucosuria and ketonuria.

Continuous observation of the level of consciousness, state of hydration, and vital signs is essential.

Laboratory investigations should be made every 2 - 4 hours for:

1. Blood sugar level: Initial sample should be made in the laboratory, then bedside analysis can be simply made by using the commercial strips ***(Hemoglukotest)*** and capillary blood samples. However, accuracy of this test should be checked every 6 -8 hours by the standard laboratory method.
2. Serum electrolytes (Na, K).
3. Acid-base balance by blood gas analysis (pH, $PaCO_2$ and HCO_3).
4. Urine analysis for sugar and acetone.

When an infection seems to be a precipitating factor, blood and urine cultures should be made.

In comatose patient, **oxygen therapy** is important and a **nasogastric tube** is inserted to evacuate the stomach to avoid vomiting and aspiration.

The main lines of management are:

1. Correction of shock, acidosis and dehydration by I.V. fluids: This is the most urgent line of therapy. Treatment can be divided into 3 stages:

(a) Shock therapy: 20 ml/kg of normal saline (0.9%) is given over 1 hour. Alternatively, Ringer's lactate solution can be used.

(b) Deficit therapy: The amount needed is usually 80-100 ml/kg. Treatment is started with normal saline until blood sugar level becomes below 300 mg/dl, then the solution is changed to a glucose and saline mixture in a ratio of 1:1. Deficit therapy should be given over 10 hours. Four precautions are important:

1. Half the amount is given in first 4 hours and the other half in next 6 hours.
2. One to two hours after initiation of insulin therapy, potassium chloride solution (15%) should be added to the deficit solution in an amount of 1.5 ml for each 100 ml of the solution. This amount will make a potassium concentration of 30 mEq/liter.
3. Correction of metabolic acidosis by sodium bicarbonate is only indicated when acidosis is severe (pH below 7.15 and HCO_3 below 10 mEq/liter). A single dose of sodium bicarbonate 5% (2 ml/kg, I.V., over 10 minutes) is sufficient, as complete correction will occur with I.V. fluid therapy and insulin therapy.
4. Re-evaluation of deficit therapy should be made after 6 hours of therapy in the light of clinical and laboratory status.

(c) Maintenance therapy: It is given over the next 24 hours. The solution used is a mixture of glucose 5% and saline in a ratio of 4:1 with addition of 1 ml of potassium chloride solution 15% to each 100 ml of the mixture. Alternatively, kadalex and saline in a 4:1 ratio can be used. The amount given equals the daily requirements (see I.V. fluid therapy). An extra-amount of 10- 20% may be added if polyuria is continuing.

2. Correction of hyperglycemia by insulin therapy: Once I.V. fluids are started and shock therapy is going on, insulin therapy is initiated. Insulin is given by the *low-dose continuous I.V. infusion method*. With this method, insulin is given through a separate I.V. line. 50 units of regular insulin are added to 500 ml saline (in this solution, each 1 ml contains 0.1 unit of insulin). Therapy is started by continuous infusion in a dose of 0.1 unit/kg/hour (i.e.1 ml/kg/hour) without a bolus dose. For instance, if the patient weight is 25 kg, give the infusion at a rate of 25 ml/hour, i.e. 8 drops/minute. When blood glucose level reaches below 300 mg/dl, the dose of insulin can be reduced to 0.05 unit/kg/hour for several hours then the infusion is discontinued and regular insulin is given in a dose of 0.2 - 0.4 unit/kg, every 6 - 8 hours, subcutaneous.

3. Control of the precipitating infection: When an infection seems to be the precipitating factor, a broad-spectrum antibiotic as ampicillin is given I.V. in a dose of 50-75 mg/kg/day, in 4 divided doses. Therapy can be adjusted according to the results of cultures.

At the end of this stage, the patient should be conscious, fully hydrated and ready for oral intake.

B) Management during the post-acidotic phase

During this phase, management includes the following lines:

1. Diet: As soon as the patient is ready to take fluids by mouth, sips of water may be given for few hours until it is evident that vomiting and gastric dilatation are unlikely to occur. Then, soft and liquid diet is given at 3 hours intervals, consisting mainly of carbohydrates as fruit juice, gelatin desserts, skimmed milk and fat free ice cream. Within 1 - 2 days on this regimen, the child should be ready for average diet.

2. Insulin therapy: Regular insulin is given subcutaneous is a dose of 0.2-0.4 unit/kg, every 6 - 8 hours, before meals. Blood glucose level should be monitored before and 2 hours after each meal and insulin dosage can be adjusted to keep blood sugar level between 100 - 180 mg/dl. This regimen is continued for 24 hours after the child is already eating average diet. The total daily dose is then calculated to be used as a guide for dosage in the next phase of management. It is important to remember that in case of children presenting with classic symptoms, but without ketoacidosis, the insulin requirements are less and the dose of regular insulin is only 0.1 - 0.2 unit/kg, every 6-8 hours, before meals. For these children, this stage can be called "the phase of initial adjustment".

3. Close observation: Clinical and laboratory check up are essential to avoid insulin shock (hypoglycemia) or return to hyperglycemia. Treatment of infections, if present, is continued during this phase.

At the end of this stage, which usually takes 2-3 days, the patient is receiving average diet and is ready for the next phase.

C) Lifelong management

During the first few days of this long-term phase, the patient is kept in hospital for adjustment of insulin dosage and for education of parents and the child about the different aspects of management.

1. Insulin therapy: Lifelong therapy with *insulin subcutaneous injections* is the only drug therapy for management of type I diabetes. Oral hypoglycemic drugs used in adults are not suitable.

(a) Dosage: The daily dose of insulin is calculated by one of 2 methods:
- Empirical dosage: 0.5 -1.0 unit/kg/day. Always start with the low dosage and increase or decrease by 10% according to blood sugar levels.
- Two thirds of the total daily dose during the post-acidotic phase or phase of initial adjustment.

(b) Types of insulin: Intermediate insulin form ***(Insulin Monotard)*** and regular insulin ***(insulin Actrapid)*** are used in different ways according to the used schedule or regimen (see below).

(c) Schedule or regimens of injections: There are 2 regimens:

- ***Three-injection regimen:*** The total daily dose is divided into 3 equal doses, given subcutaneous, 30 minutes before the 3 major meals.

* The breakfast dose is ¾ intermediate insulin and ¼ regular insulin.
* The lunch dose is only regular insulin.
* The supper or evening dose is ½ intermediate insulin and ½ regular insulin.

This regimen provides better control of blood sugar with less incidence of hypoglycemia or hyperglycemia.

- ***Two-injection regimen:*** The total daily dose is divided into 2 unequal doses:

* 2/3 of the calculated daily dose is given 30 minutes before breakfast.
* One third of the calculated dose is given 30 minutes before evening meal (Each dose is 2/3 intermediate insulin and one-third regular insulin).

This regimen would provide poor coverage for lunch and early morning and would increase the risk of hypoglycemia at midmorning and early night. However, this regimen is easier than the 3-injection regimen and is sometimes preferred by parents and the child.

(d) Techniques of injections: Special disposable syringes with fine needles are available for insulin therapy (insulin syringe). The syringe is calibrated in units (1 ml = 100 units).

- The subcutaneous injection is made at 90° to the plane of the skin.

- The site of injection should be changed every time and rotating sites are used to reduce the incidence of lipodystrophic changes.
- Parents and the child should be trained about the drawing of insulin and the technique of injection. Regular insulin should be always drawn first.
- Older children, above 10 years, can often give the injections by themselves.

(e) Monitoring the response: The main objective of insulin therapy is to keep fasting blood sugar level between 80 -120 mg/dl, and to keep postprandial level between 100 - 150 mg/dl.

- At home, parents and the child should learn the ***self-monitoring of glucose and ketones in urine.*** Commercial strips (Several trade names) are available and can be easily used. The urinary testing should be made 4 times/day, before each major meal, and on second void specimen (A specimen taken half an hour after evacuation of bladder).
- ***Self-monitoring of blood glucose (SMBG),*** by the child or the parents at home, 3-4 times per day is preferable than the urine monitoring. It is done by blood glucose strips that are read either visually or by glucometer. SMBG allows rapid detection of hypoglycemia or hyperglycemia especially during days of illness.

(f) Adjustment of dosage: As a rule, any increase or decrease in insulin dosage is made in the range of 10 - 15%. Adjustment can be made according to blood sugar level, diet, exercise or infections.

- ***Blood sugar level:*** At home, changes in dosage are made on the light of *self-monitoring of blood glucose (SMBG)*. With hyperglycemia, the dose of insulin is increased (0.5 unit/kg for each 100 mg/dl above the target glucose level, which is 100-140 mg/dl). On the other hand, if hypoglycemia is present (blood sugar level is below 60 mg/dl), the dose of insulin is decreased by 10 -15%.

- ***Diet:*** Adjustment of insulin dosage may be also made in response to change in amount or type of food. Heavy meals or high carbohydrate meals necessitate an increase in insulin dosage. On the other hand, fasting requires a decrease in insulin dosage.

- ***Exercise:*** The major complication of exercise is hypoglycemia and a reduction in dosage by 10 –15% may be needed.

- ***Infections:*** With infections, hyperglycemia is a risk and insulin dosage may be increased by 10 - 15%.

- A reliable index of long-term control is provided by measurement of hemoglobin A_1C (normal level is 3 - 5% of total). It gives an idea about the glycemic control during the last 4 months.

2. Diet and nutritional requirements: The basic principle is to provide full nutritional requirements to achieve a normal growth:

(a) Number of meals: Three major meals every day, preferably given at fixed times, e.g. 8 a.m., 2 p.m. and 8 p.m. Two additional snacks may be given between meals.

(b) Composition of food: Generally, 50% of the nutritional requirements are carbohydrates, 30% fats and 20% proteins:
- The carbohydrates given should be mainly derived from the complex carbohydrates which are slowly digested and absorbed as starchy products (rice, macaroni, potatoes etc...). On the other hand, sweetened foods and products containing simple sugars, as sugar, sweets, candies, and carbonated beverages (as Pepsi and Seven-up) should be discouraged, because they are rapidly absorbed and may cause wide fluctuations in metabolic control. Alternatively, sugar-free beverages (as Pepsi Diet) can be used and artificial non-nutritive sweeteners can be added to drinks as tea. It is important to realize that sweets and cakes are not completely forbidden, but the rule is to limit their intake.
- Fats given should be mainly of plant origin. Butter and other animal fats used for cooking are substituted by vegetable oils as corn oil and soups of animal origin are substituted by vegetable soups. Animal proteins with high fat content as fatty meats are replaced by those with low fat content as chickens and fish.
- Diets with high fiber content as vegetables and fresh fruits are encouraged. Legumes, grains and cereals are particularly useful.

(c) Adjustment in meal planning: It is important to emphasize that meals should not be designed on the basis of hard and rigid rules, but the individual needs and desires of each child should be considered. Multiple restrictions will eventually create feelings of anxiety and rejection. With vigorous exercise, the increased food intake will help in prevention of hypoglycemia.

3. Exercise: Diabetic children should not be made to feel different from other children. All forms of activity and exercise, including the competitive sports, should be encouraged. Each child can eventually determine the optimal level of his activity. Hypoglycemia (major complication) can be avoided by:
- Increased food intake prior to exercise, or
- Reduced insulin dosage by 10 - 15% prior to exercise.

4. Emotional support: Diabetes, as any other chronic illness, puts the entire family under emotional stress. The genetic origin of type I diabetes usually creates the feelings of anxiety and guilt in one or both parents. Patience, understanding and continuous support by the physician can help in solving many of these problems.

* **Prognosis:** Type I diabetes is not a benign disease. The life expectancy of these children is approximately two thirds that of general population. Vascular, ocular and renal diseases are the most serious late complications, and they are directly related to the duration of diabetes and the degree of glycemic control.

Practical example

A child, 7 years old (24 kg) presenting with diabetic ketoacidosis (shock, acidosis, dehydration and blood glucose level of 750 mg/dl).

1. INITIAL MANAGEMENT

- *Hospitalization + Oxygen therapy + Nasogastric tube*
- *Blood sample for investigations*
- *Two I. V. lines (fluid therapy + insulin therapy)*

A) I.V. fluid therapy

* ***Shock therapy:*** 480 ml saline over one hour (160 drops/minute)

* ***Deficit therapy:*** 24 x 80 = 1920 ml (over 10 hours)

Start with saline until blood sugar level comes below 300 mg/dl then change to glucose 5% and saline in a ratio of 1:1. Add potassium chloride 15% (1.5 ml for each 100 ml of solution).

- Give 50% (960 ml) over the first 4 hours (240 ml/hour or 80 drops/ minute) and the other 50% over the next 6 hours (160 ml/hour or 53 drops/minute).
- If pH is below 7.15 give $NaHCO_3$ 5% (2 ml/kg, I.V., over 10 minutes).

* ***Maintenance therapy:*** 1600 ml (of kalalex and saline mixture in a ratio of 4: 1) over 24 hours (66 ml/hour or 22 drops/minute).

B) Insulin therapy

Add 50 units insulin to 500 ml saline and give through a separate line at a rate of 24 ml/hour (8 drops/minute). Continue infusion until blood sugar level is below 300 mg/dl and decrease the rate to 4 drops/minute for several hours then discontinue and give 5-6 units subcutaneous every 6-8 hours before meals.

2. DURING THE POST-ACIDOTIC PHASE

- Start oral feeding and proceed to regular diet.
- Give insulin 5 - 6 units subcutaneous every 6 - 8 hours before meals. Adjust dosage according to blood sugar level.

3. LONG-TERM MANAGEMENT

A) Insulin therapy: The daily dose (0.5 unit/kg) is 0.5 x 24 = 12 units.

One of 2 regimens can be used:

* ***Three-injection regimen:*** Three equal doses (each is 4 units), given 30 minutes before the 3 major meals.

- Breakfast dose: 3 units intermediate (Monotard) + one unit regular (Actrapid).
- Lunch dose: 4 units regular insulin (Actrapid).
- Evening dose: 2 units intermediate (Monotard) + 2 units regular (Actrapid).

(Self-monitoring of blood glucose should be made at least 3 times per day).

* ***Two-injection regimen:*** Two unequal doses, given 30 minutes before breakfast and before evening meal.
-Two thirds (8 units), 30 minutes before breakfast.
(5.5 units insulin Monotard + 2.5 units insulin Actrapid).

- One third (4 units), 30 minutes before evening meal.
(2.5 units insulin Monotard + 1.5 units insulin Actrapid

B) Diet planning.

C) Exercise.

Another example

A child, 5 years old (18 kg) presenting with polyuria and polydipsia. Fasting blood glucose is 150 mg/dl and 2 hours post prandial is 210 mg/dl.

These clinical and laboratory findings are diagnostic of type I diabetes. Management in this case is the management of the **new onset diabetes without ketoacidosis.**

A) Insulin therapy: The daily dose (0.5 unit/kg) is 0.5 x 18 = 9 units.

One of 2 regimens can be used:

* ***Three-injection regimen:*** Three equal doses (each is 3 units), given 30 minutes before the 3 major meals.

- Breakfast dose: 2 units intermediate (Monotard) + one unit regular (Actrapid).
- Lunch dose: 3 units regular insulin (Actrapid).
- Evening dose:1.5 units intermediate (Monotard) + 1.5 units regular (Actrapid).

(Self-monitoring of blood glucose should be made at least 3 times per day).

* ***Two-injection regimen:*** Two unequal doses, given 30 minutes before breakfast and before evening meal.
-Two thirds (6 units), 30 minutes before breakfast.
(4 units insulin Monotard + 2 units insulin Actrapid).

- One third (3 units), 30 minutes before evening meal.
(2 units insulin Monotard + 1 units insulin Actrapid

(During the first week or two of management, self-monitoring of blood glucose should be made before and 2 hours after every injection. After proper control of dosage, monitoring should be done at least 3 times per day).

B) Diet planning.

C) Exercise.

11

Immune Disorders

1. Infantile Eczema.
2. Urticaria.
3. Henoch-Schonlein Vasculitis.
4. Juvenile Rheumatoid Arthritis.
5. Systemic Lupus Erythematosus.
6. Immunodeficiency.

1. Infantile Eczema

Atopic dermatitis or infantile eczema is a common allergic skin disorder of infants and young children. The condition usually presents in early infancy as erythematous patches on the cheeks. The lesions may extend to involve the face, neck and extremities. Exudation, crusting and scaling usually occur and itching is severe.

In many cases, the onset of illness is related to introduction of certain foods as cows milk, cereals or eggs to the infant's diet.

Remission usually occurs at the age of 3 -5 years.

Management of atopic dermatitis includes the following aspects:

1. Topical corticosteroid therapy: This is the main line of treatment. A steroid ointment ***(Dermatop or Perderm ointment)*** is used for dry lesions and steroid creams ***(Dermatop or Perderm cream)*** are more suitable for wet lesions. Twice applications per day are sufficient. The duration of therapy depends on the severity of the condition and it may take weeks for an adequate control. Several preparations of topical steroids are available, but some precautions are important:

— Prolonged topical steroid therapy may lead to skin atrophy.
— The extremely potent flourinated preparations should not be applied to the face.
— When an infection is present, topical antibiotics should not be used, but systemic antibiotics are indicated (see topically-applied medications).

2. Oral antihistamines: The use of a highly sedating antihistamine, as promethazine ***(Phenergan surup)*** is preferable to get adequate control of itching. However, any other antihistamine can be used. In infants, the use of a drop form as dimetindene ***(Fenistil drops)*** is preferable. Fingernails should be kept cut as short as possible to break the itch-scratch-itch cycle. Restraints for the elbows to keep the hands away from the face are sometimes necessary to prevent scratching at night (see antihistamines).

3. Control of the environmental and triggering factors: Clothes should be made of smooth cotton, and wool should be avoided. Similarly, the infant should not be allowed to crawl on wool carpets. Bed covers and bed sheets should be made of cotton. Hot humid environment will lead to sweating and aggravation of the disease. Irritant soaps should be avoided. If bathing appears to worsen the condition, it should be kept at minimum. Foods that make itching worse should be eliminated from the diet.

2. Urticaria

Urticaria is a common allergic skin disorder. Diagnosis is easily made by presence of the characteristic skin lesion. It is circumscribed erythematous raised skin lesions (wheals), which may be localized or generalized. In papular urticaria, the lesions are papular or papulovesicular and are mainly present over extremities (see pediatric clinical diagnosis).

Management of urticaria includes the following aspects:

1. Oral antihistamines: Although the condition usually subsides spontaneously over few days, antihistamines are required for the symptomatic relief of itching and for rapid control of the skin lesions. Several drugs are available and therapy can be started with any of them as clemastine ***(Tavegyl),*** mequitazine ***(Primalan),*** promethazine ***(Phenergan)*** or dimedindene ***(Fenistil)***. The average duration of therapy is only few days. (For accurate dosage, see antihistamines).

2. Other anti-allergic drugs: In severe cases of confluent urticaria, the use of an oral corticosteroid as **dexamethasone** ***(Orazone)*** may be needed for few days in a dose of 0.5 mg/kg/day. In extremely severe cases, rapid symptomatic relief can be achieved by subcutaneous **adrenaline** injection in a dose of 0.01 mg/kg. Practical dosage is 0.1 ml/kg of diluted solution (1 ml + 9 ml saline).

3. Local measures: In localized lesions as in papular urticaria, topical application of calamine lotion ***(Caladryl, Calazol or Calamyl lotion)*** twice daily may be used as a soothing antipruritic measure.

4. Avoidance of further exposure to the causative agent: When a definite reliable history suggests that the condition follows a particular food, that food should be temporarily eliminated. Otherwise, the common mistake of avoiding some foods as eggs, banana or chocolates in every case should be avoided. If a particular drug seems responsible, it should be discontinued. In papular urticaria, avoidance of exposure to insect bites is important.

5. Treatment of chronic urticaria: If urticaria persists for more than 6 - 8 weeks, other drugs are usually necessary. **Hydroxyzine** ***(Atarax tablets, 10 mg)*** is the drug of choice. It is given in a dose of 0.5 mg/kg every 6 hours. Other drugs as **cimetidine** ***(Tagamet tablets, 200 mg)*** or **chlorpromazine** ***(Largactil)*** may be also useful. Cimetidine is an H_2-antihistamine, mainly used in treatment of peptic ulcer and gastroesophageal reflux.

3. Henoch-Schonlein Vasculitis

Fortunately, the prognosis of most cases of Henoch-Schonlein vasculitis is excellent and patients will recover completely within few days to several weeks. However, **prolonged follow-up** is important because renal involvement may be delayed and only appears after control of other manifestations.

Management of Henoch-Schonlein vasculitis depends on the involved systems:

1. In patients with skin rash and arthritis only, treatment is only symptomatic. Aspirin is usually sufficient to control fever and joint pains. When the rash is pruritic or angioneurotic oedema appears, antihistamines may be also used.

2. In patients with gastrointestinal manifestations, the early use of corticosteroids is important to prevent serious complications as intestinal hemorrhage or perforation. Prednisone is given orally in a dose of 1-2 mg/kg/day, and this is usually associated with dramatic improvement. The dose is then decreased and the drug is discontinued within several days to few weeks.

3. In patients with renal involvement, management depends on the degree of affection. Patients with mild azotemia and mild hypertension need no therapy, while patients with severe oliguria and moderate to severe hypertension are managed as those with acute renal failure. Corticosteroids may be also used for severe nephritis. Although most cases recover within weeks, some patients may develop a chronic renal disease.

4. In patients with CNS manifestations as convulsions or motor weakness, the use of corticosteroids is also indicated. Although CNS manifestations are rare, serious sequelae may occur.

4. Juvenile Rheumatoid Arthritis

Juvenile rheumatoid arthritis (JRA) is the main cause of chronic arthritis in children. Diagnosis is usually made on clinical basis and depends on the presence of persistent arthritis for more 6 weeks and after exclusion of other causes of arthritis (See Pediatric Clinical Diagnosis).

Management of juvenile rheumatoid arthritis includes the following aspects:

1. Anti-inflammatory therapy: It aims to control the symptoms (pain, swelling, limitation of movements) and to preserve joint functions. It is important to realize that a full therapeutic response of any used drug may take several weeks or months and the drug is not labeled as "insufficient" except after an adequate trial of, at least, 6 weeks.

(a) Nonsteroidal anti-inflammatory drugs (NSAIDs): Among the different available drugs, few only are suitable for pediatric use. **Acetylsalicylic acid** ***(Alkasprine or Alexoprine forte tablets, 300 mg)*** was for decades the initial drug of choice but recently its use is gradually replaced by other NSAIDs. It is given orally in a dose of 100 mg/kg/day, divided into 3 doses, after meals. The total daily dose should not exceed 3 gm. Buffered preparations are preferable to minimize gastric irritation and antacids can be added for those with stomachache. Once a full therapeutic response is achieved, the daily therapy may be continued for several months or even years. Chronic salicylate therapy is relatively safe. The drug should be kept out of reach of the child to avoid accidental poisoning. **Naproxen** ***(Naprosyn tablets, 250 mg and 500 mg)*** can be used in a dose of 10-20 mg/kg/day in 2-3 divided doses. **Diclofenac** ***(Voltaren, Antiflam or Cataflam tablets, 25 mg and 50 mg)*** is safe and probably more effective than aspirin. It is given in a dose of 1-3 mg/kg/day, in 2 -3 divided doses. **Ibuprofen** ***(Brufen or Marcofen tablets, 200 mg and 400 mg)*** is also safe and probably as effective as aspirin. It is given in a dose of 30-50 mg/kg/day, in 2-3 divided doses. **Tolmetin** ***(Tolectin OR Rumatol capsules, 200 mg and 400 mg)*** is recently available and can be given in a dose of 20-30 mg/kg/day , in 2-3 divided doses. **Ketoprofen** is recently available in a syrup form ***(Ketofan syrup, 12.5 mg/5 ml and tablets, 25 mg)*** and it is given in a dose of 1-3 mg/kg/day, in 2 divided doses. As the response of an individual patient to therapy is different, failure of an adequate trial with one drug is an indication to try another one or to add methotrexate in low dosage (see below).

(b) Methotrexate: Recently, low dose of methotrexate (10 mg/m^3 once weekly, oral or 25 mg/m^3 once weekly, subcutaneous) is considered the safest, most effective and least toxic second-line drug. It is recommended as a second drug for those with inadequate response to nonsteroidal anti-inflammatory drugs.

(c) Corticosteroids: Its use should be limited to the following 3 indications:
- Severe systemic disease not responding to an adequate trial of aspirin.
- Congestive heart failure secondary to myocarditis.
- Iridocyclitis not responding to topical steroids.

It is important to remember that corticosteroids should not be used for relief of joint manifestations alone. Although a dramatic response usually appears, several problems will arise (1) they do not produce permanent remission or prevent joint damage, (2) prolonged use will impair growth, (3) increasing doses will be required to obtain the same effect. Eventually, they will be like a "trap" from which the patient cannot go out. In rare situations where steroids seem necessary, prednisone is used in a dose of 1 mg/kg/day, to be changed to the alternate-day therapy with the lowest effective dosage (see corticosteroids).

2. Physiotherapy: The child can usually determine his own level of activity. Bed rest is not indicated and moderate activities as tricycle riding and swimming are useful and should be encouraged. Exercise programs should be carried out at home every day. Night splints for knees and wrists may help to prevent deformities. Prolonged immobilization of joints should be avoided. Occasional intra-articular injection of steroids may be useful. In advanced cases, orthopedic procedures as synovectomy or total replacement may be indicated.

3. Reassurance and support: Both parents and the child should be reassured that in spite of the chronic nature of illness, the ultimate prognosis is good for most patients. Children should be encouraged to attend school, share in activities and live as normal life as possible. Continuous reassurance and support can be of great value.

Practical examples

1. A child, 6 years old (20 kg) with polyarticular JRA.

RI Alkasprine OR Alexoprine forte tablets (300 mg).
2 tablets, 3 times daily (after meals).

OR RI Naprosyn OR Naprofen tablets (250 mg).
One tablet, twice daily.

OR RI Voltaren OR Antiflam OR Cataflam tablets (25 mg).
One tablet, twice daily.

OR RI Tolectin OR Rumatol capsules (200 mg).
One capsule, twice daily.

(Evaluate the response after 6 weeks of onset of therapy).

2. A child, 6 years old (20 kg) not responding to NSAIDs for 6 weeks.

Add oral methotrexate (10 mg/m^2 one every week) = 10 x 0.7 = 7 mg.
(Surface area of 20 kg = 0.7 m^2).

RI Methotrexate tablets (2.5 mg).
Three tablets, oral, once every week.

5. Systemic Lupus Erythematosus

Unlike juvenile rheumatoid arthritis, which has a good prognosis, systemic lupus erythematosus in children is a potentially fatal disease. Prognosis depends mainly on the degree of renal, cardiac and CNS involvement. As no curative treatment is available, therapy is mainly aiming to suppress the various clinical manifestations and to maintain the general well being of the patient. As the various manifestations may appear sequentially over years, **prolonged follow-up and repeated evaluation** are essential.

Management of systemic lupus erythematosus includes the following:

1. Systemic lupus without nephritis: In patients presenting with a mild disease and without clinical nephritis, manifestations can be suppressed by aspirin or other nonsteroidal anti-inflammatory drugs as in JRA. However, NSAIDs should be used with caution in patients with SLE because they are more susceptible to hepatotoxicity. Skin lesions are suppressed by topical steroids. Prolonged follow-up for possible development of nephritis is important.

2. Systemic lupus with nephritis: In patients with clinical nephritis, corticosteroids are used to suppress the renal disease and to return serum complement level to normal. **Prednisone** is given orally in a dose of 1-2 mg/kg/day, in divided doses. With prolonged therapy, the alternate-day therapy should be considered to minimize the side effects (see corticosteroids). Severely ill patients may require pulse intravenous corticosteroid therapy (30 mg/kg/dose, over 60 minutes once per day, for 3 days). Intermittent high-dose intravenous therapy in combination with low-dose daily oral therapy can be used as an alternative regimen. In patients not responding adequately to corticosteroids alone, the use of anticancer drugs as cyclophosphamide or chlorambucil may be considered, but the use of these drugs should be limited to physicians experienced in pediatric oncology. Recently, intravenous pulse therapy with **cyclophosphamide** ***(Endoxan or Cytoxan vial, 100 mg and 200 mg/amp.)*** is quite effective is severe cases. Dialysis and renal transplantation may be considered for severe lupus nephritis.

3. Systemic lupus with CNS involvement: Manifestations of CNS involvement as convulsions usually occur during episodes of exacerbation. During these episodes, the dose of prednisone should be increased to adequately suppress the manifestations. It is important to remember that CNS lupus must be differentiated from CNS infections and steroid psychosis.

4. Frequent re-evaluation: Lupus is a lifelong illness, so frequent and clinical and laboratory evaluation is the most important aspect of management. Early recognition and treatment of disease flare is essential to patient outcome.

6. Immunodeficiency

The immunologic system has 3 main components:

1. Lymphocyte system: It is the system responsible for the specific immune response. It has 2 functioning cells:

(a) B-cell lymphocytes: These cells secrete the immunoglobulins:

- Immunoglobulin M (IgM): Antibodies of the initial response.
- Immunoglobulin G (IgG): Antibodies of the late response.
- Immunoglobulin A (IgA): Antibodies of the mucosal surfaces. They protect the mucosa of the respiratory passages and the intestinal tract.

The main functions of these 3 classes are:

1. Protection against bacterial infections.
2. Initial prevention of viral infections.
3. Local protection of respiratory and intestinal mucous membranes.

(b) T-cell lymphocytes: There are, at least, 5 types of T cells:

- T-helper (T_4): They help B-cells to secrete immunoglobulins.
- T-suppressor (T_8): They prevent overproduction of immunoglobulins.
- T-killer (T-cytotoxic): They combine with the antigen to kill the invading organisms (mainly, acid fast bacilli, viral infections and fungal infections).
- T-lymphokine producing (T-ampilifier): They secrete chemical mediators, which affect other cells to amplify the immunologic response.
- T-memory (T-affector): They memorize the body on re-exposure to respond much more quickly. This phenomenon of immunological memory is used in active immunization against infectious diseases.

2. Phagocyte system: It is the system responsible for the nonspecific immune response: It has 2 functioning cells:

(a) Neutrophils: These cells are the circulating phagocytes. They migrate to the site of infection, engulf the bacteria and destroy them.

(b) Monocytes: These cells rapidly leave the circulation to the tissues where they mature to become the fixed tissue phagocytes (macrophages). The syndrome of "overwhelming infections following splenectomy" occurs due to lack of these cells.

The main function of the phagocyte system is the nonspecific protection against bacterial infections.

3. Complement system: It has both direct and indirect effects:

- Direct effect: It causes lysis of the microorganisms through producing a hole in the cell membrane. All components (Cl to C9) share in this process.
- Indirect effect: It helps other immune cells. It produces chemotactic factors

to neutrophils and monocytes, helps B-cells to produce antibodies and T-cells to initiate the cytotoxic effect.

Immunodeficiency is frequently considered in case of unusually recurrent severe infections. Fortunately, disorders of immunodeficiency are relatively uncommon. In the majority of cases of clinical suspicion, laboratory investigations reveal an intact immunologic system, and the recurrent infections were simply caused by repeated exposure to infectious agents. It is important to emphasize that any child should not be labeled as having **"poor resistance to infection"** except after laboratory confirmation of immunodeficiency.

A) B-cell immunodeficiency (Humoral immunodeficiency)

The possibility of B-cell deficiency is usually considered in case of unusually recurrent severe **bacterial infections,** as recurrent pneumonia, meningitis or septicemia.

1. Laboratory diagnosis of B-cell deficiency is made by both screening and diagnostic tests:

(a) Screening tests: Measurement of **serum immunoglobulins** is the most commonly used test. Normal serum levels are:
- Ig G: 700 - 1400 mg/dl.
- IgM: 30 - 200 mg/dl.
- IgA: 15 - 200mg/dl.

Notice: In early infancy, IgM may be normally as low as 15 mg/dl and IgA as low as 3 mg/dl.

Wrong interpretation of results is a common mistake in practice and the diagnosis should be only made with the following criteria:
- IgG deficiency: With serum level of IgG below 200 mg/dl.
- IgM deficiency: With serum level of IgM below 10 mg/dl.
- IgA deficiency: With serum level of IgA below 5 mg/dl.
- Panhypogammaglobulinemia: IgG + IgM ± IgA below 250 mg/dl.
- Intestinal loss of proteins: low IgG + IgA with normal IgM.

It is important to remember that a normal level of IgA does not exclude secretory IgA deficiency.

(b) Diagnostic tests: These tests are indicated when screening tests are inconclusive or equivocal. Quantitative **enumiration of B-cells** in peripheral blood can be made depending on the presence of surface receptors for immunoglobulins or complement. **Specific antibody response** can be also tested by measuring the antibody response to a specific antigen, as antigens of immunization procedures. Complete evaluation of B-cell function may necessitate **measurement of T_4 and T_8 activity.** Low T_4 and high T_8 may be the cause of increased susceptibility to bacterial infections.

2. Treatment of proven B-cell deficiency is made by immunoglobulin therapy. Plasma therapy is occasionally used.

(a) Immunoglobulin therapy: It is indicated in case of total deficiency of IgG, IgA and IgM (Panhypogammaglobulinemia). A loading dose of 1.4 ml/kg is given I.M., followed by 0.7 ml/kg every 4 weeks, ***(Gammaglobulin amp.,2 ml).*** The loading dose can be fractionated over few days and the maintenance dose can be also divided into 2 doses (every 2 weeks). It is important to emphasize that patients with selective IgA deficiency should not receive immunoglobulins because fatal anaphylactic reactions may occur due to the presence of circulating anti-IgA antibodies. Fortunately, a significant number of these patients improve spontaneously with time.

(b) Plasma therapy: It can be used as an alternative to immunoglobulin therapy. The main advantage is that the donor can be immunized to give a specific antibody. Hepatitis with repeated transfusions largely limits its use.

B) T-cell immunodeficiency (Cellular immunodefeciency)

The possibility of T-cell deficiency is considered in case of severe recurrent **viral or fungal infections.** Persistent oral moniliasis after an adequate therapy or chronic mucocutaneous candidiasis should raise the suspicion. Systemic illness following BCG or measles vaccination is another clinical presentation.

1. Laboratory diagnosis is made by both screening and diagnostic tests:

(a) Screening tests: As T-cell lymphocytes account for 80% of peripheral blood lymphocytes, so **total lymphocyte count** reflects the T-lymphocytes to a greater extent than B-lymphocytes, if the total lymphocyte count is below 1200/cmm, T-cell deficiency is suspected, However, lymphopenia may be secondary to viral infections, autoimmune diseases or malignancy. On the other hand, normal or elevated counts may be obtained in patients with severe cellular immunodeficiency, **Delayed hypersensitivity skin tests** (as tuberculin test) is another simple screening test. Positive skin test (induration of 5 mm or more) indicates a normal T-cell function, however, negative skin tests are inconclusive of T-cell dysfunction especially in infants. **Lateral chest x-ray** to demonstrate the thymus shadow is a third simple screening test. Absent thymus shadow suggests T-cell deficiency.

(b) Diagnostic tests: These tests are indicated when screening tests are suggestive. Quantitative **enumiration of T-cells** in peripheral blood is the main test. Mature T-cells have the property of binding in vitro to sheep erythrocytes to form rosettes (Erythrocyte rosette-formation). Normally, the percentage of rosette-forming cells is 80%. Counts below 20% indicate a primary T-cell immunodeficiency, while counts between 20-45% occur with viral infections, autoimmune diseases or malignancy. The **subpopulations of T-cells** can be also enumerated by monoclonal antibodies. The **several T-cell functions** can

be also assessed by different assays. T-cytotoxic activity is assessed by a test called **"cell mediated lympholysis".** T-helper, T-suppressor, T-lymphokine producing and T-memory functions can be also assessed by specific tests.

2. Treatment of proven T-cell deficiency is made through different methods, but generally it is not as simple as B-cell deficiency:

(a) Immunocompetent bone marrow transplantation: It is indicated in Digeorge syndrome, Nezelof syndrome and severe combined immuno-deficiency. Evidence of successful transplantation appears after 2-6 week where the total lymphocyte count increases and synthesis of immunoglobulins starts. The major risk is the development of graft versus host disease in 30-50% of cases where the donor's T-lymphocytes become cytotoxic to host cells.

(b) Fetal thymus transplantation: It is used as an alternative to bone marrow transplantation. The fetal thymus is inserted surgically in a pocket between rectal fascia and muscle.

(c) Transfer factor therapy: It is used in chronic mucocutaneous candidiasis and Wiskott Aldrich syndrome. It is derived from leukocyte lysate of skin test positive donors. It has the capacity to increase the number of T-cells and convert skin test negative to positive.

(d) Thymosin therapy: This thymic hormone is derived from extracts of calf thymus. It is capable of restoring thymic function and is used as an alternative to bone marrow transplantation when no histocompatible donors are available. Allergic reactions may occur and necessitate discontinuation of therapy.

C) Phagocyte immunodeficiency (Leukocyte disorders)

The possibility of leukocyte disorders is considered in case of severe recurrent bacterial infections of the skin and lungs. Some clinical manifestations may suggest a particular disease, as:

- Hepatosplenomegaly may suggest chronic granulomatous disease.
- Partial albinism suggests Chediak-Higashi syndrome.
- Chronic eczema and red hair suggests JOB syndrome.
- Situs inversus suggests Kartagener syndrome.

1. Laboratory diagnosis of leukocyte disorders is made through evaluation of leukocyte number and functions:

(a) Neutrophil count: Neutropenia (count below 2000/cmm) is the basic defect in familial neutropenia and cyclic neutropenia. Bone marrow examination reveals reduced neutrophilic precursors (hypoplastic neutropenia). Compensatory monocytosis and eosinophilia is usually present. Presence of abnormal leukocyte giant granules is characteristic of Chediak-Higashi. These granules appear as greenish brown cytoplasmic inclusions in neutrophils, monocytes and eosinophils.

(b) Cytochemical tests of leukocyte functions: Several cytochemical tests can be made to evaluate the leukocyte function:

— Nitroblue tetrazolium Test (NBT test): Failure to reduce the nitroblue tetrazolium dye is diagnostic of chronic granulomatous disease. The test is also valuable for detection of asymptomatic mothers who also fail to reduce the dye.

— Myeloperoxidase test: The test is defective in patients with myeloperoxidase deficiency.

— Leukocyte alkaline phosphatase test: The test is defective in patients with deficient leukocyte alkaline phosphatase.

(c) Tests of chemotaxis: Defective migration of neutrophils and monocytes from the bone into the circulation is the basic defect in Lazy leukocyte syndrome. In Job syndrome, the chemotaxis is defective and the level of immunoglobulin E is markedly elevated. In kartagener syndrome, the chemotaxis is defective and the diary function of the respiratory tract is also defective (immotile cilia syndrome).

2. Treatment of leukocyte disorders depends primarily on vigorous antibiotic therapy to control the infection. Therapy should be guided by the appropriate cultures. Leukocyte transfusion is also considered during episodes of infection. Surgical drainage of abscesses is also important. Bone marrow transplantation may be considered in severe cases.

D) Complement immunodeficiency

The possibility of complement deficiency is considered in recurrent severe bacterial infections especially with gonococcal and pneumococcal infections. Generalized seborrheic dermatitis or systemic lupus-like illness should also suggest a disorder of the complement system.

1. Laboratory diagnosis of deficiencies can be made by both screening and diagnostic tests. **Hemolytic complement assay (CH50)** is the mainly used screening test and it depends on the ability of the 9 components to interact and lyse the antibody-coated erythrocytes. The dilution of the serum, which lyses 50% of cells, determines the end point. In congenital deficiencies, the values are almost zero, while in acquired deficiencies, values vary according to the severity of the underlying disease. Determination of serum complement concentration is also available for all components, and can diagnose selective deficiencies of any component.

2. Treatment of complement system disorders depends on regular **plasma infusion**. Specific therapy by administration of purified components of complement is not available and carries the risk of inducing antibodies to them. Vigorous antibiotic therapy is important to control infections and immunization against common infections should be also considered.

7. Immune Stimulants

Several products are available in the market and manufacturers claim that these products have a stimulatory effect on immune system and they reduce the incidence of infections. However, the efficacy of these products is not evaluated or approved by FDA and with best results, they claim an effect but they do not claim cure, i.e. they can be used as a co-medication with other drugs but not used alone as a monotherapy. The most commonly used products are the following:

• **Lyophilized bacterial lysate: 3.5 mg/day ... oral (for children).**
7.0 mg/day ... oral (for adults).

It is a mixture of bacterial lysate of several organisms including hemophilus influenza, diplococcus pneumonia, streptococcus pyogens and viridans, staphylococcus aureus and klebsiella pneumonia. Manufacturers claim that the product stimulates T-lymphocyte and salivary IgA. Double-blind studies have shown that the drug increases the resistance towards respiratory tract infections and reduces in particular their incidence, severity and risk of recurrence.

The drug can be used, as a *co-medication* in treatment of respiratory infections or it can be used as a *prophylactic drug* against respiratory tract infections in those with unusually recurrent infections. The dose for prophylaxis is one capsule daily for 10 days per month for 3 months.

* Available preparations are:

RI Broncho-Vaxom capsules for children (3.5 mg).
RI Broncho-Vaxom capsules for adults (7.0 mg).

The pediatric capsules can be opened and the contents may be poured into milk or juice. Children over 6 years can take the adult capsules.

• **Echinacea extract: 100 - 200 mg ... oral ... 1-3 times daily.**

Echinacea is a herbal product with presumed stimulatory effect on immune system. Manufacturers claim that it stimulates the immune system through inhibitory effect on hyaluronidase enzyme, which is known as infection spreading factor. Other claimed mechanisms include stimulation of release of interferon and potentiation of phagocytic powers.

The drug can be used, as a *co-medication* in treatment of respiratory infections. Studies in adults have shown that the drug reduces the number of colds by 15% but no proven efficacy in children.

* Available preparations are:

RI Immulant OR Echinacea syrup (90 mg).
RI Immulant OR Fluran capsules (200 mg).
RI Immunvita capsules (210 mg).
RI Immunvita OR Mulone drops.

With the drop form, the dose is 15 drops 2-3 times per day.

Drug Index (Generic Names)

Published Books

- Pediatric Clinical Diagnosis
- Practical Pediatric Therapy
- Basic Clinical Pediatrics
- Basic Pediatric Radiology
- Pediatric Critical Care
- CT Scan in Pediatrics
- Pediatric Emergency Medicine
- Short Atlas in Pediatrics
- Pediatric Common Mistakes
- Internet in Pediatric Practice
- Famous Medical Eponyms



UNIVERSITY BOOK CENTRE
8 Soliman El Halaby Street., Cairo
Tel. 25774881 - 23957807
Fax: 25897635 - Mobile 0123698600

AL-AHRAM COMMERCIAL PRESS - KALYUOB